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PATENT TRADEMARK OFFICE

CHAPTER II

**TRANSMITTAL LETTER
TO THE UNITED STATES ELECTED OFFICE (EO/US)**

(ENTRY INTO U.S. NATIONAL PHASE UNDER CHAPTER II)

INTERNATIONAL APPLICATION NO. PCT/IL99/00645	INTERNATIONAL FILING DATE 30 NOVEMBER 1999	PRIORITY DATE CLAIMED 1 DECEMBER 1998 27 JANUARY 1999
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TITLE OF INVENTION
COMPUTERIZED ADAPTIVE IMAGING

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Box PCT
Assistant Commissioner for Patents
Washington D.C. 20231
ATTENTION: EO/US

CERTIFICATION UNDER 37 C.F.R. 1.10*
(Express Mail label number is **mandatory**.)
(Express Mail certification is optional.)

I hereby certify that this correspondence and the documents referred to as attached therein are being deposited with the United States Postal Service on this date MAY 21, 2001, in an envelope as "Express Mail Post Office to Addressee," Mailing Label Number EL 728213035 US, addressed to the: Assistant Commissioner for Patents, Washington, D.C. 20231.

CONNIE YANNOTTI

(type or print name of person mailing paper)

Signature of person mailing paper

WARNING: Certificate of mailing (first class) or facsimile transmission procedures of 37 C.F.R. 1.8 cannot be used to obtain a date of mailing or transmission for this correspondence.

***WARNING:** Each paper or fee filed by "Express Mail" **must** have the number of the "Express Mail" mailing label placed thereon prior to mailing. 37 C.F.R. 1.10(b).
"Since the filing of correspondence under § 1.10 without the Express Mail mailing label thereon is an oversight that can be avoided by the exercise of reasonable care, requests for waiver of this requirement will **not** be granted on petition." Notice of Oct. 24, 1996, 60 Fed. Reg. 56,439, at 56,442.

NOTE: *The completion of those filing requirements that can be made at a time later than 30 months from the priority date results from the Commissioner exercising his judgment under the authority granted under 35 USC 371(d). The filing receipt will show the actual date of receipt of the last item completing the entry into the national phase. See 37 C.F.R. §1.491 which states: "An international application enters the national state when the applicant has filed the documents and fees required by 35 USC 371(c) within the periods set forth in § 1.494 and § 1.495."*

WARNING: *Where the items are those which can be submitted to complete the entry of the international application into the national phase are subsequent to 30 months from the priority date the application is still considered to be in the international state and if mailing procedures are utilized to obtain a date the express mail procedure of 37 C.F.R. §1.10 must be used (since international application papers are not covered by an ordinary certificate of mailing - See 37 C.F.R. §1.8.*

NOTE: *Documents and fees must be clearly identified as a submission to enter the national state under 35 USC 371 otherwise the submission will be considered as being made under 35 USC 111 37 C.F.R. § 1.494(f).*

1. Applicant herewith submits to the United States Elected Office (EO/US) the following items under 35 U.S.C. 371:

- a. ☒ This express request to immediately begin national examination procedures (35 U.S.C. 371(f)).
- b. ☒ The U.S. National Fee (35 U.S.C. 371(c)(1)) and other fees (37 C.F.R. § 1.492) as indicated below:

2.Fees

CLAIMS FEE	(1) FOR	(2) NUMBER FILED	(3) NUMBER EXTRA	(4) RATE	(5) CALCULATIONS
[]*	TOTAL CLAIMS	37 - 20 =	17	x \$ 18.00 =	\$ 306.00
	INDEPENDENT CLAIMS	8 - 3 =	5	x \$ 80.00 =	400.00
	MULTIPLE DEPENDENT CLAIM(S) (if applicable) + \$270.00				
BASIC FEE**	<input type="checkbox"/> U.S. PTO WAS INTERNATIONAL PRELIMINARY EXAMINATION AUTHORITY Where an International preliminary examination fee as set forth in § 1.482 has been paid on the international application to the U.S. PTO: <input type="checkbox"/> and the international preliminary examination report states that the criteria of novelty, inventive step (non-obviousness) and industrial activity, as defined in PCT Article 33(2) to (4) have been satisfied for all the claims presented in the application entering the national stage (37 CFR 1.492(a)(4)) \$100.00 <input type="checkbox"/> and the above requirements are not met (37 CFR 1.492(a)(1)) \$690.00 <input checked="" type="checkbox"/> U.S. PTO WAS NOT INTERNATIONAL PRELIMINARY EXAMINATION AUTHORITY Where no international preliminary examination fee as set forth in § 1.482 has been paid to the U.S. PTO, and payment of an international search fee as set forth in § 1.445(a)(2) to the U.S. PTO: <input type="checkbox"/> has been paid (37 CFR 1.492(a)(2)) \$710.00 <input type="checkbox"/> has not been paid (37 CFR 1.492(a)(3)) \$1,000.00 <input checked="" type="checkbox"/> where a search report on the international application has been prepared by the European Patent Office or the Japanese Patent Office (37 CFR 1.492(a)(5)) \$860.00				
	Total of above Calculations				1,566.00
SMALL ENTITY	Reduction by ½ for filing by small entity, if applicable. Affidavit must be filed. (note 37 CFR 1.9, 1.27, 1.28)				-
	Subtotal				
	Total National Fee				\$1,566.00
	Fee for recording the enclosed assignment document \$40.00 (37 CFR 1.21(h)). (See Item 13 below). See attached "ASSIGNMENT COVER SHEET".				
TOTAL	Total Fees enclosed				\$1,566.00

*See attached Preliminary Amendment Reducing the Number of Claims.

- i. ☒ A check in the amount of \$1,566.00 to cover the above fees is enclosed.
 ii. ☐ Please charge Account No. _____ in the amount of \$ _____.
 A duplicate copy of this sheet is enclosed.

****WARNING:** "To avoid abandonment of the application the applicant shall furnish to the United States Patent and Trademark Office not later than the expiration of 30 months from the priority date: * * * (2) the basic national fee (see § 1.492(a)). The 30-month time limit may not be extended." 37 C.F.R. § 1.495(b).

WARNING: If the translation of the international application and/or the oath or declaration have not been submitted by the applicant within thirty (30) months from the priority date, such requirements may be met within a time period set by the Office. 37 C.F.R. § 1.495(b)(2). The payment of the surcharge set forth in § 1.492(e) is required as a condition for accepting the oath or declaration later than thirty (30) months after the priority date. The payment of the processing fee set forth in § 1.492(f) is required for acceptance of an English translation later than thirty (30) months after the priority date. Failure to comply with these requirements will result in abandonment of the application. The provisions of § 1.136 apply to the period which is set. Notice of Jan. 3, 1993, 1147 O.G. 29 to 40

3. ☒ A copy of the International application as filed (35 U.S.C. 371(c)(2)):

NOTE: Section 1.495 (b) was amended to require that the basic national fee and a copy of the international application must be filed with the Office by 30 months from the priority date to avoid abandonment "The International Bureau normally provides the copy of the international application to the Office in accordance with PCT Article 20. At the same time, the International Bureau notifies applicant of the communication to the Office. In accordance with PCT Rule 47.1, that notice shall be accepted by all designated offices as conclusive evidence that the communication has duly taken place. Thus, if the applicant desires to enter the national stage, the applicant normally need only check to be sure the notice from the International Bureau has been received and then pay the basic national fee by 30 months from the priority date." Notice of Jan. 7, 1993, 1147 O.G. 29 to 40, at 35-36. See item 14c below.

- a. ☐ is transmitted herewith.
 b. ☐ is not required, as the application was filed with the United States Receiving Office.
 c. ☒ has been transmitted
 i. ☒ by the International Bureau.
 Date of mailing of the application (from form PCT/IB/308): _____.
 ii. ☐ by applicant on _____
 Date

4. ☒ A translation of the International application into the English language (35 U.S.C. 371(c)(2)):
 a. ☒ is transmitted herewith.
 b. ☐ is not required as the application was filed in English.
 c. ☐ was previously transmitted by applicant on _____
 Date
 d. ☐ will follow.

5. [X] Amendments to the claims of the International application under PCT Article 19 (35 U.S.C. 371(c)(3)):

NOTE: The Notice of January 7, 1993 points out that 37 C.F.R. § 1.495(a) was amended to clarify the existing and continuing practice that PCT Article 19 amendments must be submitted by 30 months from the priority date and this deadline may not be extended. The Notice further advises that: "The failure to do so will not result in loss of the subject matter of the PCT Article 19 amendments. Applicant may submit that subject matter in a preliminary amendment filed under section 1.121. In many cases, filing an amendment under section 1.121 is preferable since grammatical or idiomatic errors may be corrected." 1147 O.G. 29-40, at 36.

- a. ☐ are transmitted herewith.
- b. ☐ have been transmitted
- i. ☐ by the International Bureau.
- Date of mailing of the amendment (from form PCT/IB/308): _____.
- ii. ☐ by applicant on _____.
Date
- c. ☒ have not been transmitted as
- i. ☒ applicant chose not to make amendments under PCT Article 19.
- Date of mailing of Search Report (from form PCT/ISA/210): JUNE 22, 2000.
- ii. ☐ the time limit for the submission of amendments has not yet expired.
The amendments or a statement that amendments have not been made will be transmitted before the expiration of the time limit under PCT Rule 46.1.

6. [X] A translation of the amendments to the claims under PCT Article 19 (38 U.S.C. 371(c)(3)):

- a. ☐ is transmitted herewith.
- b. ☐ is not required as the amendments were made in the English language.
- c. ☒ has not been transmitted for reasons indicated at point 5(c) above.

7. [X] A copy of the international examination report (PCT/IPEA/409)
[X] is transmitted herewith.
[] is not required as the application was filed with the United States Receiving
Office.

8. [] Annex(es) to the international preliminary examination report

- a. ☐ is/are transmitted herewith.
- b. ☐ is/are not required as the application was filed with the United States Receiving Office.

9. [] A translation of the annexes to the international preliminary examination report

- a. [] is transmitted herewith.
- b. [] is not required as the annexes are in the English language.

10. ☒ An oath or declaration of the inventor (35 U.S.C. 371(c)(4)) complying with 35 U.S.C. 115
- a. ☐ was previously submitted by applicant on _____
Date
- b. ☐ is submitted herewith, and such oath or declaration
- i. ☐ is attached to the application.
- ii. ☐ identifies the application and any amendments under PCT Article 19 that were transmitted as stated in points 3(b) or 3(c) and 5(b); and states that they were reviewed by the inventor as required by 37 C.F.R. 1.70.
- c. ☒ will follow.

Other document(s) or information included:

11. ☒ An International Search Report (PCT/ISA/210) or Declaration under PCT Article 17(2)(a):
- a. ☒ is transmitted herewith.
- b. ☐ has been transmitted by the International Bureau.
Date of mailing (from form PCT/IB/308): _____.
- c. ☐ is not required, as the application was searched by the United States International Searching Authority.
- d. ☐ will be transmitted promptly upon request.
- e. ☐ has been submitted by applicant on _____
Date
12. ☒ An Information Disclosure Statement under 37 C.F.R. 1.97 and 1.98:
- a. ☐ is transmitted herewith.
Also transmitted herewith is/are:
- ☐ Form PTO-1449 (PTO/SB/08A and 08B).
- ☐ Copies of citations listed.
- b. ☒ will be transmitted within THREE MONTHS of the date of submission of requirements under 35 U.S.C. 371(c).
- c. ☐ was previously submitted by applicant on _____
Date
13. ☐ An assignment document is transmitted herewith for recording.

A separate ☐ "COVER SHEET FOR ASSIGNMENT (DOCUMENT) ACCOMPANYING NEW PATENT APPLICATION" or ☐ FORM PTO 1595 is also attached.

14. ☒ Additional documents:
- a. ☐ Copy of request (PCT/RO/101)
 - b. ☒ International Publication No. WO 00/33250
 - i. ☒ Specification, claims and drawing
 - ii. ☐ Front page only
 - c. ☐ Preliminary amendment (37 C.F.R. § 1.121)
 - d. ☒ Other

FORM PCT/IPEA/416

15. ☒ The above checked items are being transmitted
- a. ☒ before 30 months from any claimed priority date.
 - b. ☐ after 30 months.
16. ☐ Certain requirements under 35 U.S.C. 371 were previously submitted by the applicant on _____, namely:
- _____
- _____
- _____

AUTHORIZATION TO CHARGE ADDITIONAL FEES

WARNING: Accurately count claims, especially multiple dependent claims, to avoid unexpected high charges if extra claims are authorized.

NOTE: "A written request may be submitted in an application that is an authorization to treat any concurrent or future reply, requiring a petition for an extension of time under this paragraph for its timely submission, as incorporating a petition for extension of time for the appropriate length of time. An authorization to charge all required fees, fees under § 1.17, or all required extension of time fees will be treated as a constructive petition for an extension of time in any concurrent or future reply requiring a petition for an extension of time under this paragraph for its timely submission. Submission of the fee set forth in § 1.17(a) will also be treated as a constructive petition for an extension of time in any concurrent reply requiring a petition for an extension of time under this paragraph for its timely submission." 37 C.F.R. § 1.136(a)(3).

NOTE: "Amounts of twenty-five dollars or less will not be returned unless specifically requested within a reasonable time, nor will the payer be notified of such amounts; amounts over twenty-five dollars may be returned by check or, if requested, by credit to a deposit account." 37 C.F.R. § 1.26(a).

☒ The Commissioner is hereby authorized to charge the following additional fees that may be required by this paper and during the entire pendency of this application to Account No. 12-0425.

☒ 37 C.F.R. 1.492(a)(1), (2), (3), and (4) (filing fees)

WARNING: Because failure to pay the national fee within 30 months without extension (37 C.F.R. § 1.495(b)(2)) results in abandonment of the application, it would be best to always check the above box.

☐ 37 C.F.R. 1.492(b), (c) and (d) (presentation of extra claims)

NOTE: Because additional fees for excess or multiple dependent claims not paid on filing or on later presentation must

only be paid or these claims cancelled by amendment prior to the expiration of the time period set for response by the PTO in any notice of fee deficiency (37 C.F.R. § 1.492(d)), it might be best not to authorize the PTO to charge additional claim fees, except possible when dealing with amendments after final action

- ☒ 37 C.F.R. 1.17 (application processing fees)
☒ 37 C.F.R. 1.17(a)(1)-(5)(extension fees pursuant to § 1.136(a).
☒ 37 C.F.R. 1.18 (issue fee at or before mailing of Notice of Allowance, pursuant to 37 C.F.R. 1.311(b))

NOTE: Where an authorization to charge the issue fee to a deposit account has been filed before the mailing of a Notice of Allowance, the issue fee will be automatically charged to the deposit account at the time of mailing the notice of allowance. 37 C.F.R. § 1.311(b).

NOTE: 37 C.F.R. 1.28(b) requires "Notification of any change in loss of entitlement to small entity status must be filed in the application . . . prior to paying, or at the time of paying . . . issue fee." From the wording of 37 C.F.R. § 1.28(b): (a) notification of change of status must be made even if the fee is paid as "other than a small entity" and (b) no notification is required if the change is to another small entity.

- [] 37 C.F.R. § 1.492(e) and (f) (surcharge fees for filing the declaration and/or filing an English translation of an International Application later than 30 months after the priority date).


 SIGNATURE OF PRACTITIONER

JULIAN H. COHEN

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COMPUTERIZED ADAPTIVE IMAGING

FIELD OF THE INVENTION

The present invention relates to imaging generally and more particularly to post acquisition image processing generally.

BACKGROUND OF THE INVENTION

Post acquisition image processing is well known in the literature. Publications which describe the general state of the art in post acquisition image processing are : Lim, J.S. "Two dimensional signal and image processing". Englewood Cliffs, NJ. Prentice Hall. (1990); Russ, J.C. "Image processing handbook". CRC Press (1992); Pratt, W.K. "Digital image processing". NY John Wiley & Sons, Inc. (1991); Rosenfeld, A. and Kak, A.C. "Digital picture processing". Academic Press. (1976); Castleman, K.R. "Digital Image Processing". Prentice-Hall Inc. Englewood Cliffs, New Jersey. (1979).

Imaging which provides information relating to refractive characteristics in a imaged volume is known for extremely limited applications. In microscopy, Smith, Nomarski and Differential Interference Contrast (DIC) imaging is known and is described in the following publications: Nomarski, G. "Microinterferometre differential a ondes polarisees". J. Phys. Radium 16:9S-11S (1955); Lang, W. "Differential-Interferenz-Miikroskopie". Carl-Zeiss, Oberkochen (1975); Inoui, S. and Spring, K.S. "Video Microscopy: the fundamentals". 2nd edition. Plenum Press, NY. (1997). Tanford, C. "Physical chemistry of macromolecules". John Wiley NY. (1961) Appendix C describes classical Rayleigh interference methods, Philpot and Svenson methods based on schlieren image, Lamm method of line displacement, and Gouy interference method all developed for determination of one dimensional refractive index variations.

Computer analysis of DIC imaging is not readily achieved. Known instances are described in the following publications: Allen, R.D., Allen, N.S. and Travis,

J.L. "Video-enhanced contrast, differential interference contrast (AVEC-DIC) microscopy: a new method capable of analyzing microtubule related motility in the reticulopodial network of *Allogromia laticollaria*." *Cell Motility* 1: 291-302 (1981); Cogswell, C.J. and Sheppard, C.J.R. "Confocal differential interference contrast (DIC) microscopy: including a theoretical analysis of conventional and confocal DIC imaging". *J. Microsc.* 165:81-101 (1992); Gelles, J., Schnapp, B.J. and Sheetz, M.P. "Tracking kinesin-driven movements with nanometre-scale precision", *Nature* 331:450-453 (1988); Hdusler, G. and Kvrner, E. "Imaging with expanded depth of focus". *Zeiss Inform.* 29: 9-13 (1987); Preza, C., Snyder, D.L. and Conchello, J-A. "Image reconstruction for three-dimensional transmitted light DIC microscopy". *SPIE* 2984:220-231 (1997); Schormann, T. and Jovin, T.M. "Contrast enhancement and depth perception in three-dimensional representations of differential interference contrast and confocal scanning laser microscope images". *J. Microsc.* 166:155-168 (1992).

Computerized ray tracing between discrete refractive and reflective surfaces is extremely well developed, but is not well known in the environment of non-homogeneous indices of refraction. This area is described in the following publications: Hecht E. and Zajac A. "Optics" 2nd ed. Addison-Wesley Reading MA (1997); Jenkins, F.A. and White, H.E. "Fundamentals of optics". McGraw-Hill, NY (1950) ch.8: Ray Tracing.

Calculation of point spread functions (PSF) is extremely well known as described in the following publication: Born M. and Wolf E. "Principles of Optics" Pergamon London (1959); Goodman J.W. "Statistical Optics" John Wiley & Sons NY (1985); Hecht E. and Zajac A. "Optics" 2nd ed. Addison-Wesley Reading MA. (1997); Gibson S.F. and Lanni F. "Diffraction by circular aperture as a model for three-dimensional optical microscopy". *Opt. Soc. Am. A* 6:1357-1367 (1989); Gibson S.F. and Lanni F. "Modeling aberrations due to mismatched layers for 3-D microscopy" *SPIE optics in complex systems* 1319:470-471 (1990); Gibson S.F. and Lanni F. "Experimental test of an analytical model of aberration in an oil-immersion objective lens used in three-dimensional light microscopy". *J. Opt. Soc. Am. A* 8:1601-1613 (1991).

Deconvolution of three dimensional microscopic images having location

independent PSF is well known and is described in the following publications, some of them authored by some of the present inventors: Jansson, P.A. ed "Deconvolution of images and spectra". Academic Press NY (1997); Agard, D.A. and Sedat, J.W. "Three-dimensional architecture of a polytene nucleus". Nature 302:676-681 (1984); Agard, D.A., Hiraoka, Y., Shaw, P. and Sedat, J.W. "Fluorescence microscopy in three dimensions". Methods in Cell Biology 30: 353-377 (1989); Castleman, K.R. "Digital Image Processing". Prentice-Hall Inc. Englewood Cliffs, New Jersey (1979). Correction of telescopic images by the use of suitably distorted mirrors and deconvolution of two dimensional telescope images having location dependent PSF are described in the following publications: Boden, A.F., Reeding, D.C., Hanisch, R.J., Mo, J. and White, R. "Comparative results with massively parallel spatially-variant maximum likelihood image restoration". Bul Am Astr. Soc 27:924-929 (1995); Boden, A.F., Reeding, D.C., Hanisch, R.J. and Mo, J. "Massively parallel spatially-variant maximum likelihood restoration of Hubble space telescope imagery". J Opt Soc Am A 13: 1537-1545 (1996); Jansson, P.A. ed. "Deconvolution of images and spectra". Academic Press NY (1997); Tyson R.K. "Principles of Adaptive Optics" Academic Press NY (1991). Reconstruction of blurred images from point objects is described in the following publications: Carrington, W.A., Lynch, R.M., Moore, D.W., Isenberg, G., Fogarty, K.E. and Fay, F.S. "Superresolution three-dimensional images of fluorescence in cells with minimal light exposure". Science 268:1483-1487 (1995); Femino, A.M., Fay, F.S., Fogarty, K., and Singer, R.H. "Visualization of single RNA transcripts in situ". Science 280:585-590 (1998).

SUMMARY OF THE INVENTION

The present invention seeks to provide improved apparatus and techniques for post acquisition image processing.

There is thus provided in accordance with a preferred embodiment of the present invention apparatus for computational adaptive imaging including an image information acquirer providing information relating to the refractive characteristics in a three-dimensional imaged volume, a ray tracer, utilizing the information relating to the

refractive characteristics to trace a multiplicity of rays from a multiplicity of locations in the three-dimensional imaged volume through the three-dimensional imaged volume, thereby providing a location dependent point spread function and a deconvolver, utilizing the location dependent point spread function, to provide an output image corrected for distortions due to variations in the refractive characteristics in the three-dimensional imaged volume

Preferably, the image information acquirer acquires at least two three-dimensional images of a three-dimensional imaged volume, at least one of the two three-dimensional images containing the information relating to the refractive characteristics in a three-dimensional imaged volume.

When the refractive characteristics are extractable from the image to be corrected for distortions, or are known independently, only one three-dimensional image need be acquired.

The acquirer may obtain refractive index information from DIC, for example from phase microscopy or from fluorescence -for example in DNA associated stains wherein the stain intensity is proportional to the refractive index increment.

Refractive index mapping may be applied to samples whose refractive index is known. For example this may apply to microchip wafer structures, whose geometry is known.

In accordance with a preferred embodiment of the present invention, the image acquirer acquires at least three three-dimensional images of the three-dimensional imaged volume.

Preferably, the image acquirer acquires a plurality of three-dimensional images of the three-dimensional imaged volume, each the image having a discrete wavelength band.

Alternatively, the image acquirer acquires a multiplicity of three-dimensional images of the three-dimensional imaged volume, each the image having a wavelength band which is part of a continuum represented by the wavelength bands of the multiplicity of three-dimensional images.

In accordance with a preferred embodiment of the present invention, the

ray tracer and the deconvolver utilize the information relating to the refractive characteristics in a three-dimensional imaged volume obtained from one of the three-dimensional images to correct at least another one of the three-dimensional image or itself.

The acquirer may obtain refractive index information from DIC, or from phase microscopy or from fluorescence -for example in DNA associated stains wherein the stain intensity is proportional to the refractive index increment.

Refractive index mapping may be applied to samples whose refractive index is known. For example this may apply to microchip wafer structures, whose geometry is known.

According to one embodiment of the present invention, the three-dimensional images are electromagnetic energy images. Preferably, the three-dimensional images are infrared images.

Alternatively, the three-dimensional images are non-electromagnetic images.

In accordance with a preferred embodiment of the present invention, the image acquirer receives digital image data from a digital image source and derives therefrom the information relating to the refractive characteristics in a three-dimensional imaged volume.

Preferably, the ray tracer and the deconvolver operate repeatedly over time to provide a multiplicity of output images, each corrected for distortions due to variations in the refractive characteristics in the three-dimensional imaged volume. Such a deconvolution process can be iteratively applied to the whole process to improve the estimation of the refractive index.

In accordance with one embodiment of the present invention, the output image is an acoustic image and the refractive characteristics are characteristics of a material which the passage of acoustic energy therethrough.

In accordance with an alternative embodiment of the present invention, the output image is an electromagnetic image and the refractive characteristics are characteristics of a material which the passage of electromagnetic energy therethrough.

There is also provided in accordance with a preferred embodiment of the present invention a method for computational adaptive imaging including the steps of

providing information relating to the refractive characteristics in a three-dimensional imaged volume;

ray tracing, utilizing the information relating to the refractive characteristics, a multiplicity of rays from a multiplicity of locations in the three-dimensional imaged volume through the three-dimensional imaged volume, thereby providing a location dependent point spread function; and

deconvoluting, utilizing the location dependent point spread function, thereby providing an output image corrected for distortions due to variations in the refractive characteristics in the three-dimensional imaged volume. Such a deconvolution process can be iteratively applied to the whole process to improve the estimation of the refractive index.

Preferably, the step of providing information includes acquiring at least two three-dimensional images of a three-dimensional imaged volume, at least one of the two three-dimensional images containing the information relating to the refractive characteristics in a three-dimensional imaged volume.

When the refractive characteristics are extractable from the image to be corrected for distortions, or are known independently, only one three-dimensional image need be acquired.

In accordance with a preferred embodiment of the present invention, the step of providing information includes acquiring at least three three-dimensional images of a three-dimensional imaged volume.

Preferably, the step of providing information includes acquiring a plurality of three-dimensional images of the three-dimensional imaged volume, each image having a discrete wavelength band.

In accordance with a preferred embodiment of the present invention, the step of providing information includes acquiring a multiplicity of three-dimensional images of the three-dimensional imaged volume, each the image having a wavelength band which is part of a continuum represented by the wavelength bands of the

multiplicity of three-dimensional images.

In accordance with one embodiment of the present invention, the three-dimensional images are electromagnetic energy images. Preferably, the three-dimensional images are infrared images.

In accordance with an alternative embodiment of the present invention, the three-dimensional images are non-electromagnetic images.

The refractive index may be in any medium and the imaging method may be for a generalised method for inhomogeneous media that may distort the image.

Preferably, the step of providing includes receiving digital image data from a digital image source and deriving therefrom the information relating to the refractive characteristics along a multiplicity of light paths in a three-dimensional imaged volume.

In accordance with a preferred embodiment of the present invention, the steps of providing information, ray tracing and deconvoluting operate repeatedly over time to provide a multiplicity of output images, each corrected for distortions due to variations in the refractive characteristics in the three-dimensional imaged volume. Such a deconvolution process may be iteratively applied to the whole process to improve the estimation for the refractive index map.

There is also provided in accordance with a preferred embodiment of the present invention apparatus for utilizing differential interference contrast images to provide three-dimensional refractive index information including a line integrator operating on differential interference contrast images displaying a directional derivative of refractive index of an object to invert the directional derivative thereof, thereby providing a plurality of two-dimensional representations of the refractive index of the object. Alternatively the three-dimensional refractive index map can be obtained from phase microscopy, or from fluorescence where the staining is proportional to the refractive index increment.

There is additionally provided in accordance with a preferred embodiment of the present invention apparatus for utilizing differential interference contrast images to provide three-dimensional refractive index information and also including a deconvolver

performing deconvolution of the plurality of two-dimensional representations of the refractive index of the object, thereby reducing out-of-focus contributions to the two-dimensional representations of the refractive index of the object.

There is further provided in accordance with a preferred embodiment of the present invention a method for utilizing differential interference contrast images to provide three-dimensional refractive index information including performing line integration on differential interference contrast images displaying a directional derivative of refractive index of an object to invert the directional derivative thereof, thereby providing a plurality of two-dimensional representations of the refractive index of the object. Alternatively the three-dimensional refractive index map can be obtained from phase microscopy, or from fluorescence where the staining is proportional to the refractive index increment.

Additionally in accordance with a preferred embodiment of the present invention there is provided a method for utilizing differential interference contrast images to provide three-dimensional refractive index information and also including performing deconvolution of the plurality of two-dimensional representations of the refractive index of the object, thereby reducing out-of-focus contributions to the two-dimensional representations of the refractive index of the object. Again, the three-dimensional refractive index map can be obtained from phase microscopy, or from fluorescence where the staining is proportional to the refractive index increment.

Further in accordance with a preferred embodiment of the present invention there is provided apparatus for ray tracing through a medium having multiple variations in refractive index including:

a computer employing an analytically determined path of a ray through the multiplicity of locations in the medium, for a plurality of rays impinging thereon in different directions, by utilizing known local variation of the refractive index at a multiplicity of locations in the medium.

There is additionally provided in accordance with a preferred embodiment of the present invention a method of ray tracing through a medium having multiple variations in refractive index including:

determining local variation of the refractive index at a multiplicity of locations in the medium;

analytically determining the path of a ray through the multiplicity of locations in the medium, for a plurality of rays impinging thereon in different directions. The ray tracing may also include the computation of absorptions, reflections and scattering of rays and their contributions to the imaging process.

Still further in accordance with a preferred embodiment of the present invention there is provided apparatus for confocal microscopy including:

a ray tracer, employing known variations of the refractive index in a three-dimensional sample for determining the paths of a multiplicity of rays emerging from at least one point in the sample and passing through the sample, thereby determining an aberrated wavefront for each the point; and

an adaptive optics controller utilizing the aberrated wavefront to control an adaptive optical element in a confocal microscope, thereby to correct aberrations resulting from the variations in the refractive index.

There is additionally provided in accordance with a preferred embodiment of the present invention a method for confocal microscopy including:

determining variations of the refractive index in a three-dimensional sample;

determining the paths of a multiplicity of rays emerging from at least one point in the sample and passing through the sample, thereby determining an aberrated wavefront for each the point; and

utilizing the aberrated wavefront to control an adaptive optical element in a confocal microscope, thereby to correct aberration resulting from the variations in the refractive index.

There is additionally provided in accordance with a preferred embodiment of the present invention a method for adding (computationally or physically) in the imaging path a three-dimensional medium (anti-sample) with refractive properties that correct for the distortions of the three-dimensional sample.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention will be understood and appreciated more fully from the following detailed description, taken in conjunction with the drawings in which:

Figs. 1A and 1B are respectively representations of three dimensional microscopic images of an object according to the prior art and in accordance with the present invention;

Fig. 2 is a simplified partially pictorial, partially block diagram illustration of apparatus for computational adaptive imaging constructed and operative in accordance with a preferred embodiment of the present invention;

Fig. 3 is a simplified flow chart of the operation of the apparatus for computational adaptive imaging of Fig. 2;

Fig. 4 is a simplified diagram of line integration functionality which is carried out by the apparatus of Fig. 2;

Fig. 5 is a simplified diagram of ray tracing functionality which is carried out by the apparatus of Fig. 2;

Fig. 6 is a simplified diagram of wavefront integration functionality which is carried out by the apparatus of Fig. 2; and

Fig. 7 is a simplified flow chart illustrating deconvolution functionality which is carried out by the apparatus of Fig. 2.

DETAILED DESCRIPTION OF THE INVENTION

Reference is now made to Figs. 1A and 1B, which are respectively representations of three dimensional microscopic images of an object according to the prior art and in accordance with the present invention.

It is known in the prior art to image a point source or a collection of point sources in an ideal sample displaying no substantial variation in refractive index. When an ideal optical system is focussed at slightly different depths in the sample, a three dimensional image appears, including a plurality of two-dimensional diffraction limited images designated by Roman numerals I, II, III, IV and V in Fig. 1A. The prior art, described, inter alia in the aforesaid Agard et al 1989 reference is capable of

deconvoluting the plurality of two-dimensional images I - V to a deconvoluted three dimensional image, including a single in focus two-dimensional image VI, which contains substantially all of the image intensity from images I - V and a plurality of out of focus two-dimensional images which substantially contain no image intensity

The prior art, however, does not know how to deal adequately with samples which display substantial variation in refractive index.

The present invention provides a solution to this problem, as illustrated in Fig. 1B which shows images of a non-ideal sample, such as a biological sample, displaying substantial variation in refractive index. When an ideal optical system is focussed at slightly different depths in the non-ideal sample, a three-dimensional image appears, including a plurality of two-dimensional diffraction limited images designated by Roman numerals I, II, III, IV and V in Fig. 1B. In contrast to the images appearing in Fig. 1A, it is seen that these images are extremely non-uniformly distorted due to variations in the refractive index at various locations in the sample.

The present invention, as will be described hereinbelow, is capable of deconvoluting the plurality of two-dimensional images I - V in Fig. 1B, notwithstanding their great distortions due to variations in the refractive index at various locations in the sample, to a substantially non-distorted, deconvoluted three-dimensional image, including a single in-focus two-dimensional image VI, which contains substantially all of the image intensity from images I - V and a plurality of out-of-focus two-dimensional images which substantially contain no image intensity.

Reference is now made to Fig. 2, which is a simplified partially pictorial, partially block diagram illustration of apparatus for computational adaptive imaging constructed and operative in accordance with a preferred embodiment of the present invention. The apparatus of Fig. 2 typically includes a conventional computer-controlled optical microscope 10, such as a microscope manufactured by Carl Zeiss and sold under the name Axioskop. Associated with microscope 10 there are preferably provided computer controlled filter wheels 12 and 14. Filter wheel 12 is disposed downstream of an excitation light source 16, such as a mercury arc lamp, which provides epi-illumination via a computer-controlled shutter 18 and filter wheel 12 to a dichroic

mirror 20 within the microscope 10.

Trans-illumination is provided to a sample 22, typically mounted between two slides 24 and 26, by means of a halogen light source 28 via a computer-controlled shutter 30. Depending on which of shutters 18 and 30 is open, the sample receives trans-illumination or epi-illumination so as to provide either a DIC image or a fluorescent image respectively. It is noted that DIC images conventionally require additional optical elements in the imaging light path, which are omitted from Fig. 2 for the sake of conciseness and clarity.

In accordance with a preferred embodiment of the present invention, the DIC or fluorescent image is received via computer-controlled filter wheel 14 by a digital CCD sensor 32, such as a Photometrics PXL. Preferably a polarizer is included in one of the windows of filter wheel 14 and is employed for DIC imaging.

In accordance with a preferred embodiment of the present invention, the output of the digital CCD sensor 32 is supplied to a computer 34, such as a Silicon Graphics 02 workstation which performs the following functionality:

ray tracing, utilizing information relating to the refractive characteristics in the sample, a multiplicity of rays from a multiplicity of locations in the sample through the sample, thereby providing a location dependent point spread function; and

deconvoluting, utilizing the location dependent point spread function, thereby providing an output image corrected for distortions due to variations in the refractive characteristics in the three-dimensional imaged volume.

Preferably wavefront integration is performed following the ray tracing and prior to the deconvoluting.

In accordance with a preferred embodiment of the present invention, the information relating to the refractive characteristics of the sample is provided by line integration of the DIC image.

Reference is made to Fig. 3, which is a simplified flow chart of the operation of the apparatus for computational adaptive imaging of Fig. 2. As illustrated in Fig. 3, three dimensional images from the microscope 10 and CCD 32, typically include a plurality of observed fluorescent 3D images 40 and a differential interference contrast

(DIC) 3D image 42.

In accordance with a preferred embodiment of the present invention, line integration 44 is performed on the DIC. The line integration preferably provides a 3D refractive index map 46.

In accordance with a preferred embodiment of the present invention, ray tracing 48 is performed on the 3D refractive index map 46 and the resulting wavefront is subject to wavefront integration 50, thus providing a location dependent point spread function (PSF) 52.

In accordance with a preferred embodiment of the present invention, the location dependent PSF is utilized in a deconvolution step 54 which is applied to the observed fluorescent 3D image 40.

In accordance a preferred embodiment of the invention, the deconvolution produces a corrected image, such as the image illustrated at reference VI in Fig. 1B.

Reference is now made to Fig. 4, which is a simplified diagram of line integration functionality which is carried out by the apparatus of Fig. 2. Fig. 4 illustrates a sample, such as a sphere 60 of uniform index of refraction, which differs from that of surrounding media 62. Sample 60 may be taken to represent a nucleus, while the surrounding media may be taken to represent cytoplasm. A scan line 64 illustrates the index of refraction as a function of location along line 65. The characteristic PSF of the microscope 10 operating in the DIC imaging mode is illustrated at reference numeral 66. The PSF is also illustrated by trace 68.

The output image of sample 60 of the CCD sensor 32 operating in a DIC mode is illustrated at reference numeral 70 and also by trace 72. Line integration of the output image produces an image 74 which accurately represents the original sample, seen at reference numerals 60 and 62.

It is appreciated that line integration of DIC images has two complex contributions in reality. One is the accumulation of noise in the integration and the second is the slow contribution of low-intensity out-of-focus contributions. The problem of noise is preferably alleviated by introducing a decay function in the line integration. The out-of-focus contribution can be reduced significantly by deconvoluting the

integrated DIC images.

Reference is now made to Fig. 5, which is a simplified diagram of ray tracing functionality which is carried out by the apparatus of Fig. 2. As seen in Fig. 5, it is seen that an isotropic fan of rays is drawn from every point in an imaged volume, e.g. the sample. These rays are ray traced such that their paths and phases are modified in accordance with variations in the refractive index of the sample. The result of the ray tracing is an aberrated wavefront for every point in the imaged volume.

Reference is now made to Fig. 6, which is a simplified diagram of prior art wavefront integration functionality which is carried out by the apparatus of Fig. 2. As seen in Fig. 6, for every point in the vicinity of a focus R0, an interference integral is taken over the wavefront. The integrations for all of the points in the vicinity of the focus R0 define the three-dimensional point spread function, as described inter alia in the aforesaid prior art reference to Goodman.

Reference is now made to Fig. 7, which is a simplified flow chart illustrating deconvolution functionality which is carried out by the apparatus of Fig. 2. As seen in Fig. 7, the observed image 80, such as the observed fluorescent 3D image 40 (Fig. 3) is deconvoluted using the point spread function (PSF) calculated as described hereinabove with reference to Figs. 5 and 6. It is appreciated that the location dependent PSF is preferably a multi-resolution PSF. This calculation is preferably performed in an iterative process which endeavors to provide progressively better approximations of the imaged sample.

This iterative process typically proceeds by initially defining a guessed object 82, which typically is identical to the observed image. The guessed object is convoluted with a location dependent point spread function 84, such as that derived by ray tracing and wavefront integration (Fig. 3) to produce a blurred image 86. This blurred image is compared with the observed image and a correction based on the comparison is iteratively applied to the guessed object. Following multiple iterations, the guessed object constitutes the corrected 3D image of the sample in accordance with a preferred embodiment of the present invention.

Additional technical descriptions of a preferred embodiment of the

invention appear in the following article by the inventor Z. Kam. "Microscopic Differential Interference Contrast Image Processing by Line Integration (LID) and Deconvolution". Bioimaging 6 (4): 166-176 (1998).

It will be appreciated by persons skilled in the art that the present invention is not limited to what has been particularly shown and described hereinabove. Rather the scope of the present invention includes both combinations and subcombinations of the various features described hereinabove as well as modifications and additions thereto which would occur to a person of skill in the art upon reading the foregoing description and which are not in the prior art.

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C L A I M S

We claim:

1. Apparatus for computational adaptive imaging including:
 - an image information acquirer providing information relating to the refractive characteristics in a three-dimensional imaged volume;
 - a ray tracer, utilizing the information relating to the refractive characteristics to trace a multiplicity of rays from a multiplicity of locations in the three-dimensional imaged volume through the three-dimensional imaged volume, thereby providing a location dependent point spread function; and
 - a deconvolver, utilizing the location dependent point spread function, to provide an output image corrected for distortions due to variations in the refractive characteristics in the three-dimensional imaged volume.
2. Apparatus according to claim 1 wherein the acquirer is adapted to obtain refractive index information from DIC, for example from phase microscopy or from fluorescence.
3. Apparatus according to claim 1 wherein the acquirer is adapted to utilize previously determined refractive characteristics.
4. Apparatus for computational adaptive imaging according to claim 1 and wherein the image information acquirer acquires at least two three-dimensional images of a three-dimensional imaged volume, at least one of the two three-dimensional images containing the information relating to the refractive characteristics in a three-dimensional imaged volume.
5. Apparatus according to claim 4 and wherein the image acquirer acquires at least three three-dimensional images of the three-dimensional imaged volume.
6. Apparatus according to claim 4 and wherein the image acquirer acquires a

plurality of three-dimensional images of the three-dimensional imaged volume, each the image having a discrete wavelength band.

7. Apparatus according to claim 4 and wherein the image acquirer acquires a multiplicity of three-dimensional images of the three-dimensional imaged volume, each the image having a wavelength band which is part of a continuum represented by the wavelength bands of the multiplicity of three-dimensional images.

8. Apparatus according to claim 4 wherein the image acquirer acquires a single three-dimensional image of the three-dimensional image volume.

9. Apparatus according to claim 4 and wherein the ray tracer and the deconvolver utilize the information relating to the refractive characteristics in a three-dimensional imaged volume obtained from one of the three-dimensional images to correct at least another one of the three-dimensional images.

10. Apparatus according to claim 9 wherein the ray tracer includes effects on the image of absorptions, reflections and scattering in the sample.

11. Apparatus according to claim 1, and wherein the three-dimensional images are electromagnetic energy images.

12. Apparatus according to claim 11 and wherein the three-dimensional images are infrared images.

13. Apparatus according to claim 1, and wherein the three-dimensional images are non-electromagnetic images.

14. Apparatus according to claim 1, and wherein the image acquirer receives digital image data from a digital image source and derives therefrom the information

relating to the refractive characteristics in a three-dimensional imaged volume.

15. Apparatus according to claim 1, and wherein the image acquirer, the ray tracer and the deconvolver operate repeatedly over time to provide a multiplicity of output images, each corrected for distortions due to variations in the refractive characteristics in the three-dimensional imaged volume.

16. Apparatus according to claim 1, and wherein the output image is an acoustic image and the refractive characteristics are characteristics of a material which the passage of acoustic energy therethrough.

17. Apparatus according to claim 1, and wherein the output image is an electromagnetic image and the refractive characteristics are characteristics of a material which the passage of electromagnetic energy therethrough.

18. A method for computational adaptive imaging including the steps of:
providing information relating to the refractive characteristics in a three-dimensional imaged volume;

ray tracing, utilizing the information relating to the refractive characteristics, a multiplicity of rays from a multiplicity of locations in the three-dimensional imaged volume through the three-dimensional imaged volume, thereby providing a location dependent point spread function; and

deconvoluting, utilizing the location dependent point spread function, thereby providing an output image corrected for distortions due to variations in the refractive characteristics in the three-dimensional imaged volume.

19. A method according to claim 18, for adding in the imaging path a three-dimensional medium (anti-sample) with refractive properties that correct for the distortions of the three-dimensional sample.

20. A method for computational adaptive imaging according to claim 18 and wherein the step of providing information includes acquiring at least two three-dimensional images of a three-dimensional imaged volume, at least one of the two three-dimensional images containing the information relating to the refractive characteristics in a three-dimensional imaged volume.
21. A method according to claim 20 and wherein the step of providing information includes acquiring at least three three-dimensional images of a three-dimensional imaged volume.
22. A method according to claim 20 and wherein the step of providing information includes acquiring a plurality of three-dimensional images of the three-dimensional imaged volume, each the image having a discrete wavelength band.
23. A method according to claim 20 and wherein the step of providing information includes acquiring a multiplicity of three-dimensional images of the three-dimensional imaged volume, each the image having a wavelength band which is part of a continuum represented by the wavelength bands of the multiplicity of three-dimensional images.
24. A method according to claim 18, and wherein the three-dimensional images are electromagnetic energy images.
25. A method according to claim 24 and wherein the three-dimensional images are infrared images.
26. A method according to claim 18, and wherein the three-dimensional images are non-electromagnetic images.
27. A method according to claim 18, and wherein the step of providing

includes receiving digital image data from a digital image source and deriving therefrom the information relating to the refractive characteristics along a multiplicity of light paths in a three-dimensional imaged volume.

28. A method according to claim 18, and wherein the steps of providing information, ray tracing and deconvoluting operate repeatedly over time to provide a multiplicity of output images, each corrected for distortions due to variations in the refractive characteristics in the three-dimensional imaged volume.

29. A method according to claim 28 wherein the refractive characteristics are estimated.

30. Apparatus for utilizing differential interference contrast images to provide three-dimensional refractive index information including a line integrator operating on differential interference contrast images displaying a directional derivative of refractive index of an object to invert the directional derivative thereof, thereby providing a plurality of two-dimensional representations of the refractive index of the object.

31. Apparatus for utilizing differential interference contrast images to provide three-dimensional refractive index information according to claim 30 and also including a deconvolver performing deconvolution of the plurality of two-dimensional representations of the refractive index of the object, thereby reducing out-of-focus contributions to the two-dimensional representations of the refractive index of the object.

32. A method for utilizing differential interference contrast images to provide three-dimensional refractive index information including performing line integration on differential interference contrast images displaying a directional derivative of refractive index of an object to invert the directional derivative thereof, thereby providing a plurality of two-dimensional representations of the refractive index of the object.

33. A method for utilizing differential interference contrast images to provide three-dimensional refractive index information according to claim 32 and also including performing deconvolution of the plurality of two-dimensional representations of the refractive index of the object, thereby reducing out-of-focus contributions to the two-dimensional representations of the refractive index of the object.

34. Apparatus for ray tracing through a medium having multiple variations in refractive index including:

a computer employing an analytically determined path of a ray through the multiplicity of locations in the medium, for a plurality of rays impinging thereon in different directions, by utilizing known local variation of the refractive index at a multiplicity of locations in the medium.

35. A method of ray tracing through a medium having multiple variations in refractive index including:

determining local variation of the refractive index at a multiplicity of locations in the medium;

analytically determining the path of a ray through the multiplicity of locations in the medium, for a plurality of rays impinging thereon in different directions.

36. Apparatus for confocal microscopy including:

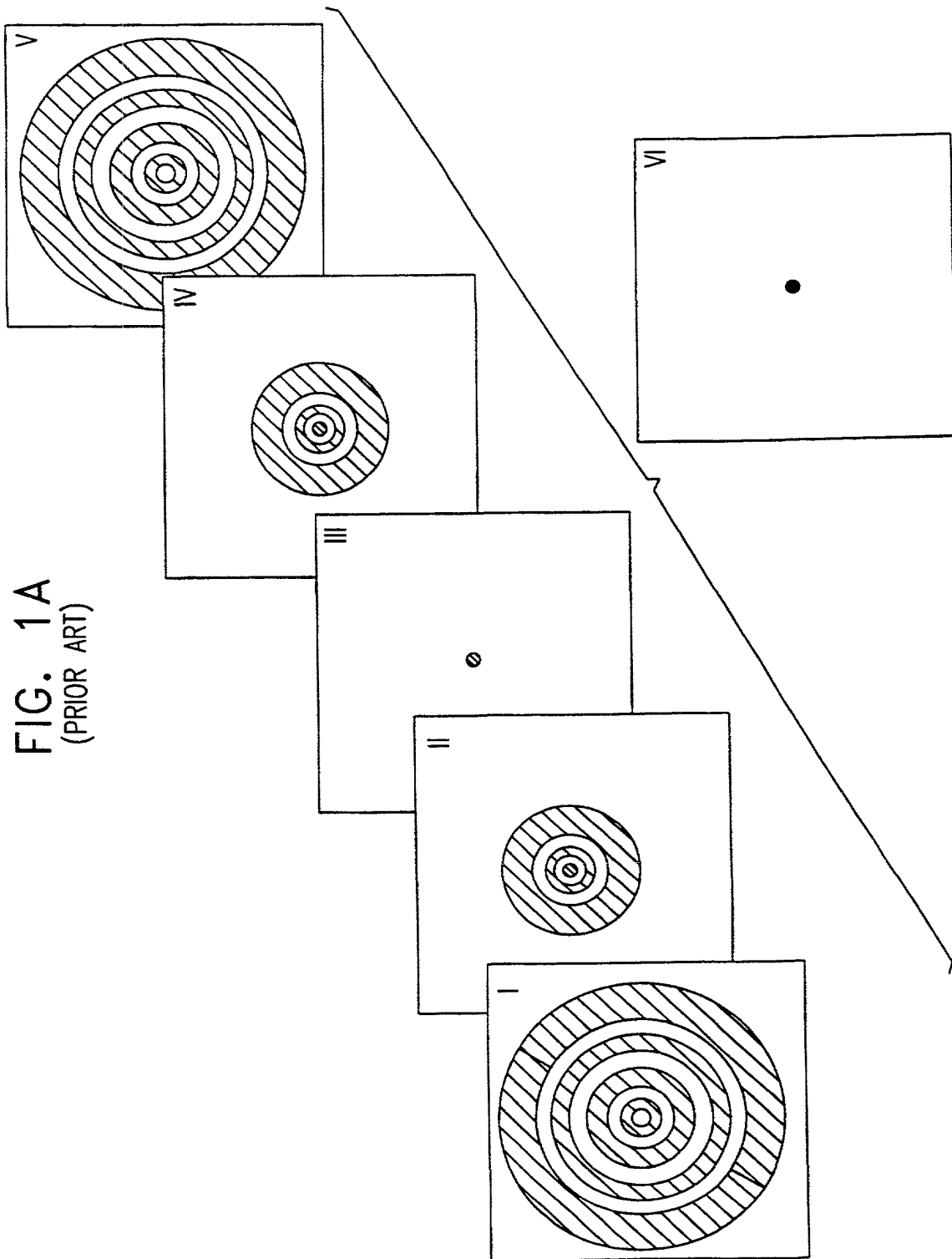
a ray tracer, employing known variations of the refractive index in a three-dimensional sample for determining the paths of a multiplicity of rays emerging from at least one point in the sample and passing through the sample, thereby determining an aberrated wavefront for each the point; and

an adaptive optics controller utilizing the aberrated wavefront to control an adaptive optical element in a confocal microscope, thereby to correct aberrations resulting from the variations in the refractive index.

37. A method for confocal microscopy including:

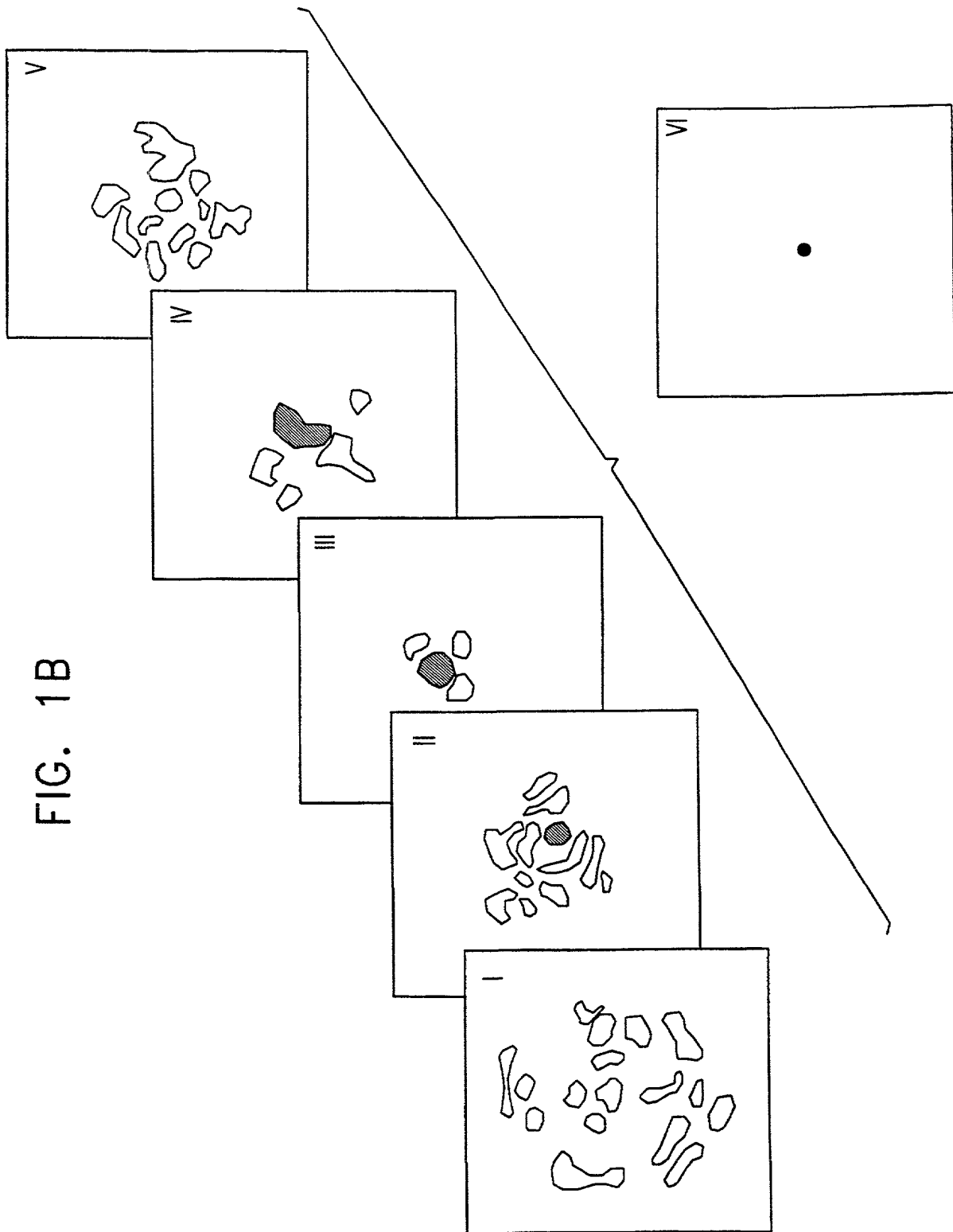
determining the paths of a multiplicity of rays emerging from at least one point in the sample and passing through the sample, thereby determining an aberrated wavefront for each the point; and

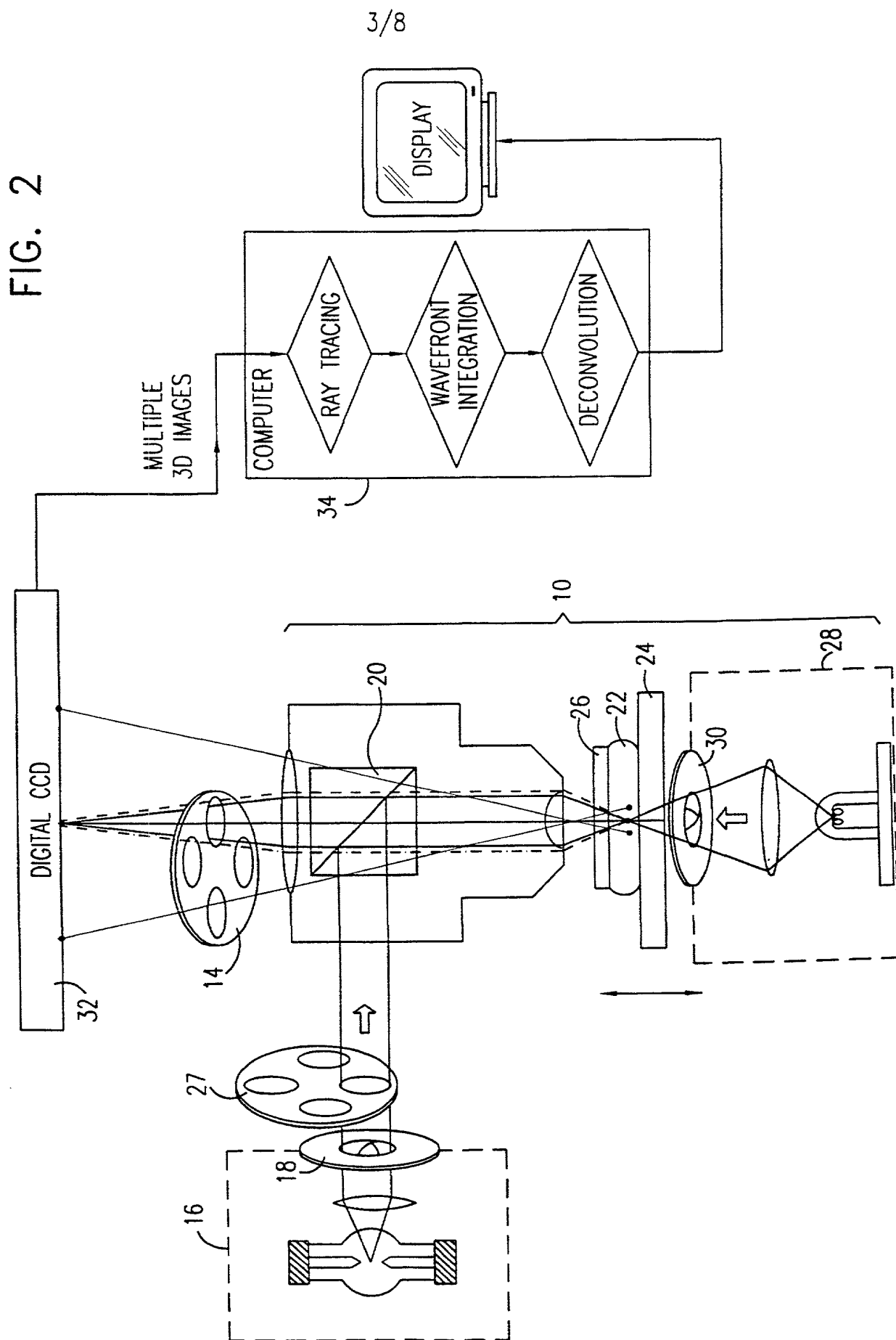
22



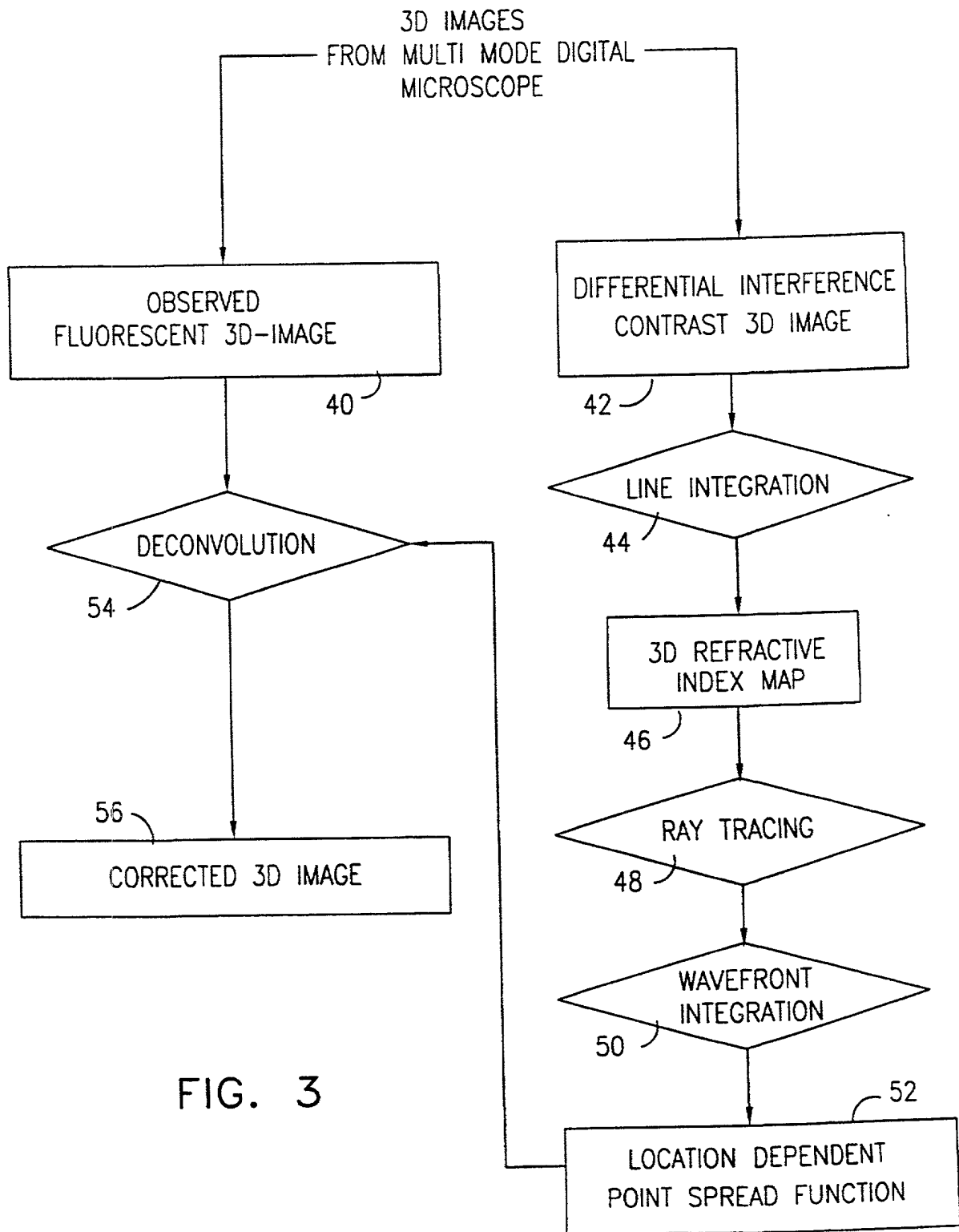
[illegible]

FIG. 1B

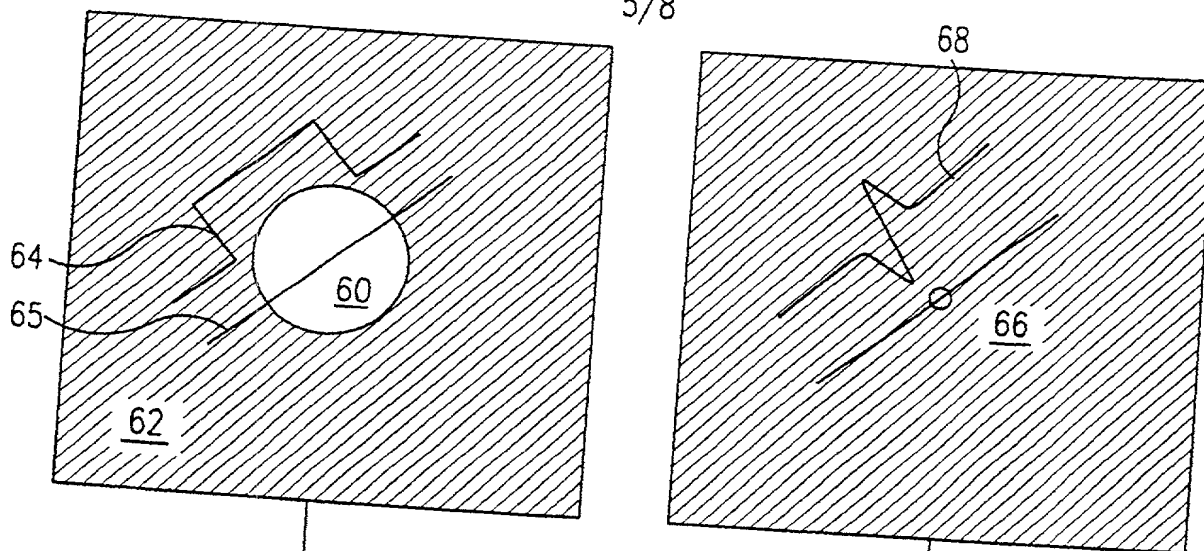




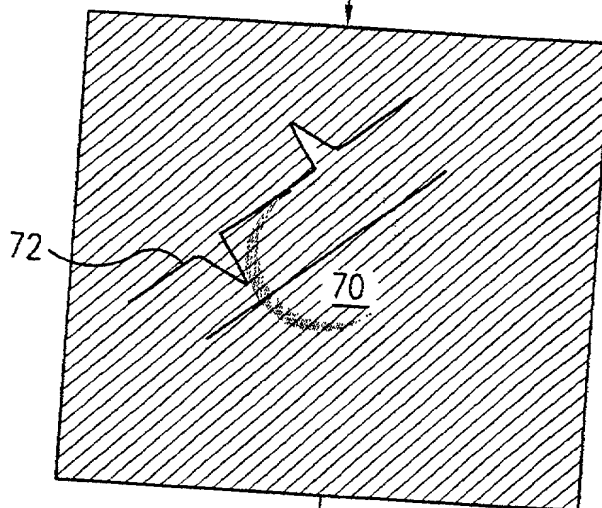
4/8



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DIFFERENTIAL INTERFERENCE CONTRAST



LINE INTEGRATION

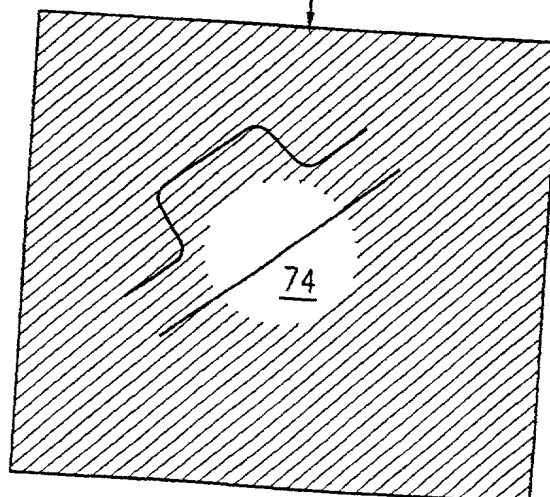


FIG. 4

FIG. 4

FIG. 5

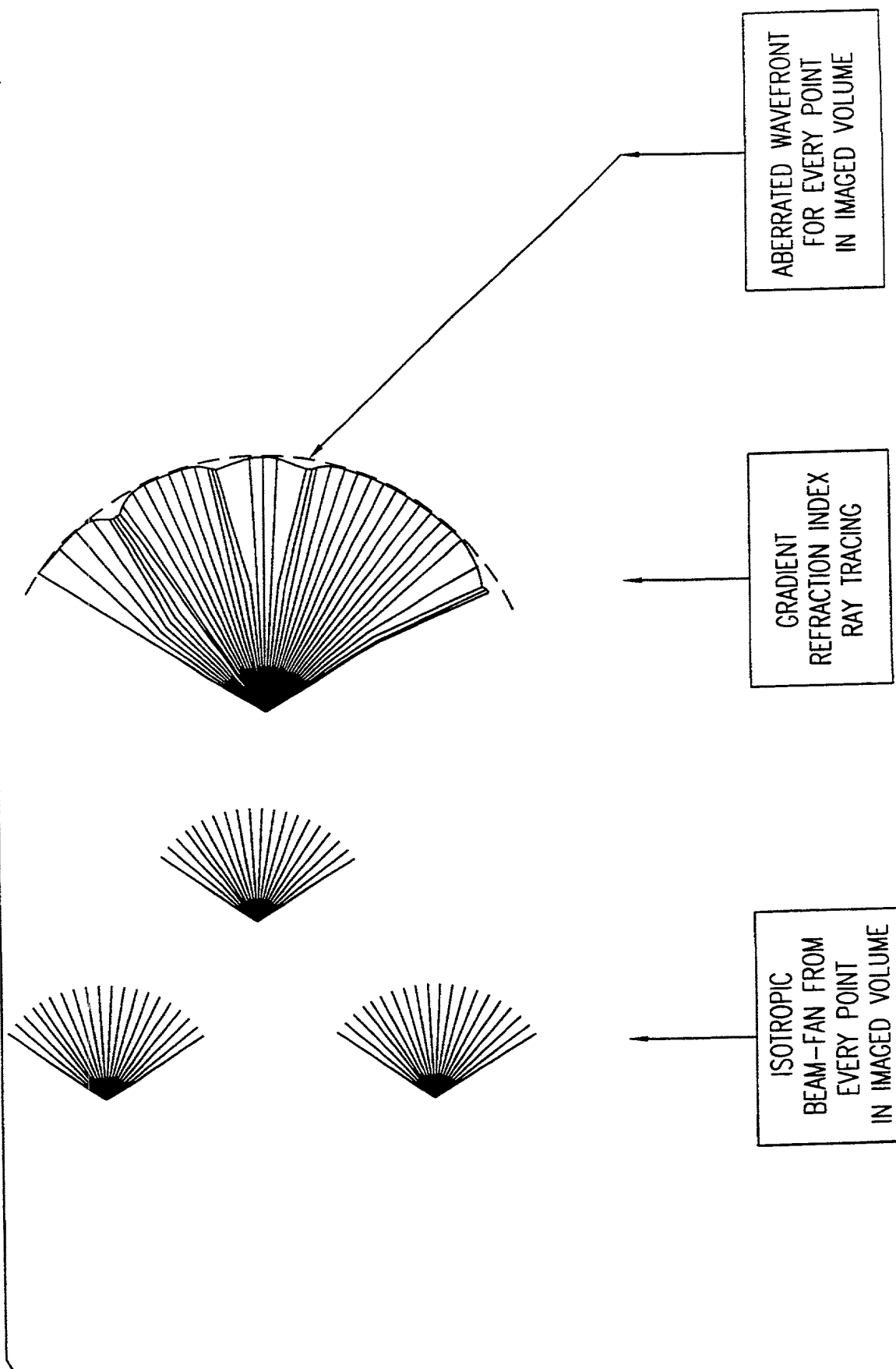
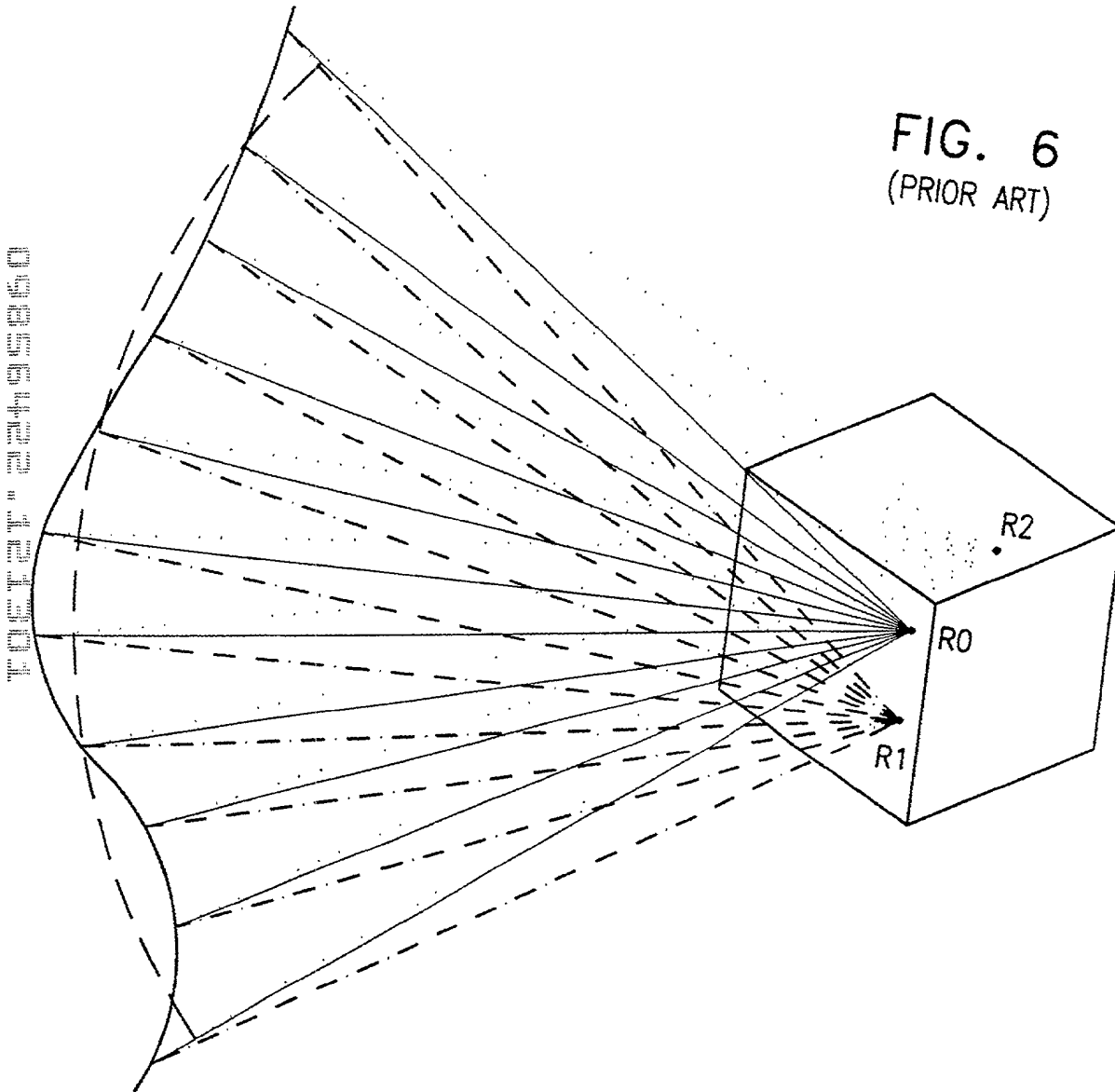
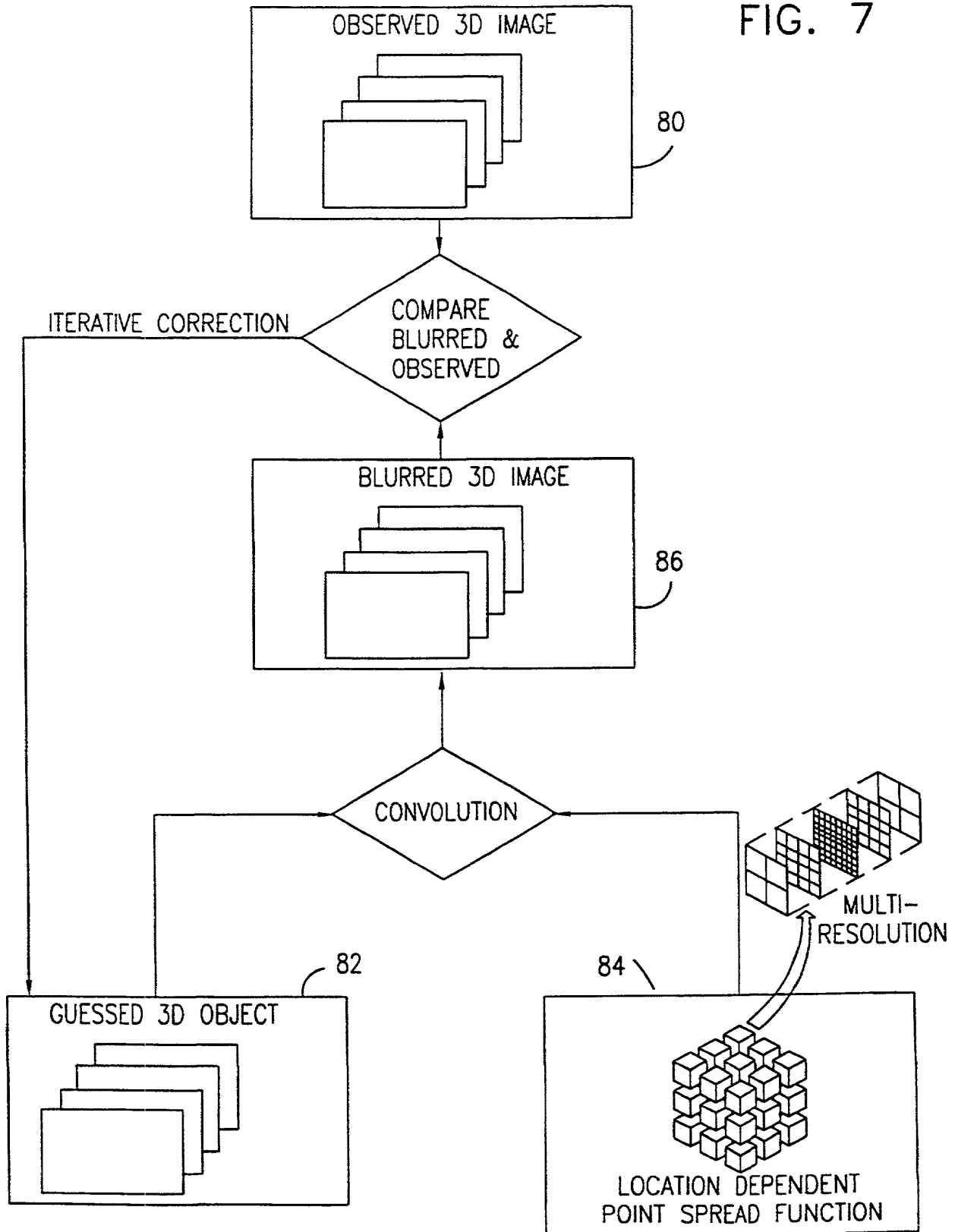


FIG. 6
(PRIOR ART)



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FIG. 7



Practitioner's Docket No. U 013475-2

PATENT

Optional Customer No. Bar Code



00140

PATENT TRADE MARK OFFICE

COMBINED DECLARATION AND POWER OF ATTORNEY

(ORIGINAL, DESIGN, NATIONAL STAGE OF PCT, SUPPLEMENTAL, DIVISIONAL, CONTINUATION, OR C-I-P)

As a below named inventor, I hereby declare that:

TYPE OF DECLARATION

This declaration is of the following type:

(check one applicable item below)

- ☐ original
☐ design

NOTE: With the exception of a supplemental oath or declaration submitted in a reissue, a supplemental oath or declaration is not treated as an amendment under 37 CFR 1.312 (Amendments after allowance), M.P.E.P. Section 714.16, 7th Ed.

- ☐ supplemental.

NOTE: If the declaration is for an International Application being filed as a divisional, continuation or continuation-in-part application, do not check next item; check appropriate one of last three items.

- ☒ national stage of PCT.

NOTE: If one of the following 3 items apply, then complete and also attach **ADDED PAGES FOR DIVISIONAL, CONTINUATION OR C-I-P**.

NOTE: See 37 C.F.R. Section 1.63(d) (continued prosecution application) for use of a prior nonprovisional application declaration in the continuation or divisional application being filed on behalf of the same or fewer of the inventors named in the prior application.

- ☐ divisional.
☐ continuation.

NOTE: Where an application discloses and claims subject matter not disclosed in the prior application, or a continuation or divisional application names an inventor not named in the prior application, a continuation-in-part application must be filed under 37 C.F.R. Section 1.53(b) (application filing requirements-nonprovisional application).

- ☐ continuation-in-part (C-I-P).

43395

INVENTORSHIP IDENTIFICATION

WARNING: *If the inventors are each not the inventors of all the claims, an explanation of the facts, including the ownership of all the claims at the time the last claimed invention was made, should be submitted.*

My residence, post office address and citizenship are as stated below, next to my name. I believe that I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter that is claimed, and for which a patent is sought on the invention entitled:

TITLE OF INVENTION

COMPUTERIZED ADAPTIVE IMAGING

SPECIFICATION IDENTIFICATION

The specification of which:

(complete (a), (b), or (c))

(a) ☐ is attached hereto.

NOTE: *The following combinations of information supplied in an oath or declaration filed on the application filing date with a specification are acceptable as minimums for identifying a specification and compliance with any one of the items below will be accepted as complying with the identification requirement of 37 C.F.R. Section 1.63:*

"(1) name of inventor(s), and reference to an attached specification which is both attached to the oath or declaration at the time of execution and submitted with the oath or declaration on filing;

"(2) name of inventor(s), and attorney docket number which was on the specification as filed; or

"(3) name of inventor(s), and title which was on the specification as filed."

Notice of July 13, 1995 (1177 O.G. 60).

(b) ☐ was filed on _____ ☐ as Application No. _____
☐ and was amended on _____ (if applicable).

NOTE: *Amendments filed after the original papers are deposited with the PTO that contain new matter are not accorded a filing date by being referred to in the declaration. Accordingly, the amendments involved are those filed with the application papers or, in the case of a supplemental declaration, are those amendments claiming matter not encompassed in the original statement of invention or claims. See 37 C.F.R. Section 1.67.*

NOTE: *"The following combinations of information supplied in an oath or declaration filed after the filing date are acceptable as minimums for identifying a specification and compliance with any one of the items below will be accepted as complying with the identification requirements of 37 C.F.R. Section 1.63:*

- (A) application number (consisting of the series code and the serial number, e.g., 08/123,456);*
- (B) serial number and filing date;*
- (C) attorney docket number which was on the specification as filed;*
- (D) title which was on the specification as filed and reference to an attached specification which is both attached to the oath or declaration at the time of execution and submitted with the oath or declaration; or*
- (E) title which was on the specification as filed and accompanied by a cover letter accurately identifying the application for which it was intended by either the application number (consisting of the series code and the serial number, e.g., 08/123,456), or serial number and filing date. Absent any statement(s) to the contrary, it will be presumed that the application filed in the PTO is the application which the inventor(s) executed by signing the oath or declaration.*

M.P.E.P. Section 601.01(a), 7th ed.

- (c) [x] was described and claimed in PCT International Application No. PCT/IL99/00645 filed on November 30, 1999 and as amended under PCT Article 19 on _____ (if any).

SUPPLEMENTAL DECLARATION (37 C.F.R. Section 1.67(b))

(complete the following where a supplemental declaration is being submitted)

[] I hereby declare that the subject matter of the

[] attached amendment

[] amendment filed on _____

was part of my/our invention and was invented before the filing date of the original application, above identified, for such invention.

ACKNOWLEDGMENT OF REVIEW OF PAPERS AND DUTY OF CANDOR

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information, which is material to patentability as defined in 37, Code of Federal Regulations, Section 1.56,

(also check the following items, if desired)

[] and which is material to the examination of this application, namely, information where there is a substantial likelihood that a reasonable Examiner would consider it important in deciding whether to allow the application to issue as a patent, and

[] in compliance with this duty, there is attached an information disclosure statement, in accordance with 37 C.F.R. Section 1.98.

PRIORITY CLAIM (35 U.S.C. Section 119(a)-(d))

NOTE: "The claim to priority must be in no special form and may be made by the attorney or agent if the foreign application is referred to in the oath or declaration as required by Section 1.63. The claim for priority and the certified copy of the foreign application specified in 35 U.S.C. Section 119(b) must be filed in the case of an interference (Section 1.630), when necessary to overcome the date of a reference relied upon by the examiner, when specifically required by the examiner, and in all other situations, before the patent is granted. If the claim for priority or the certified copy of the foreign application is filed after the date the issue fee is paid, it must be accompanied by a petition requesting entry and by the fee set forth in Section 1.17(i). If the certified copy is not in the English language, a translation need not be filed except in the case of interference; or when necessary to overcome the date of a reference relied upon by the examiner; or when specifically required by the examiner, in which event an English language translation must be filed together with a statement that the translation of the certified copy is accurate." 37 C.F.R. Section 1.55(a).

I hereby claim foreign priority benefits under Title 35, United States Code, Section 119(a)-(d) of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed.

62375

(complete (d) or (e))

- (d) ☐ no such applications have been filed.
 (e) ☒ such applications have been filed as follows.

NOTE: Where item (e) is entered above and the International Application which designated the U.S. itself claimed priority check item (e), enter the details below and make the priority claim.

**PRIOR FOREIGN/PCT APPLICATION(S) FILED WITHIN 12 MONTHS
 (6 MONTHS FOR DESIGN) PRIOR TO THIS APPLICATION
 AND ANY PRIORITY CLAIMS UNDER 35 U.S.C. SECTION 119(a)-(d)**

COUNTRY (OR INDICATE IF PCT)	APPLICATION NUMBER	DATE OF FILING DAY, MONTH, YEAR	PRIORITY CLAIMED UNDER 35 USC 119
IL	127359	1 DECEMBER 1998	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
US	09/238,225	27 JANUARY 1999	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
			<input type="checkbox"/> YES <input type="checkbox"/> NO
			<input type="checkbox"/> YES <input type="checkbox"/> NO
			<input type="checkbox"/> YES <input type="checkbox"/> NO

**CLAIM FOR BENEFIT OF PRIOR U.S. PROVISIONAL APPLICATION(S)
 (35 U.S.C. Section 119(e))**

I hereby claim the benefit under Title 35, United States Code, Section 119(e) of any United States provisional application(s) listed below:

PROVISIONAL APPLICATION NUMBER

FILING DATE

**CLAIM FOR BENEFIT OF EARLIER U.S./PCT APPLICATION(S)
 UNDER 35 U.S.C. SECTION 120**

- ☐ The claims for the benefit of any such applications are set forth in the attached
 ADDED PAGES TO COMBINED DECLARATION AND POWER OF ATTORNEY
 FOR DIVISIONAL, CONTINUATION OR CONTINUATION-IN-PART (C-I-P)
 APPLICATION.

42395

**ALL FOREIGN APPLICATION(S), IF ANY, FILED MORE THAN 12 MONTHS
(6 MONTHS FOR DESIGN) PRIOR TO THIS U.S. APPLICATION**

NOTE: If the application filed more than 12 months from the filing date of this application is a PCT filing forming the basis for this application entering the United States as (1) the national stage, or (2) a continuation, divisional, or continuation-in-part, then also complete **ADDN PAGES TO COMBINED DECLARATION AND POWER OF ATTORNEY FOR DIVISIONAL, CONTINUATION OR C+P APPLICATION** for benefit of the prior U.S. or PCT application(s) under 35 U.S.C. Section 120.

POWER OF ATTORNEY

I hereby appoint the following practitioner(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith.

(list name and registration number)

JOSEPH H. HANDELMAN, 26179

JULIAN H. COHEN, 20302

JOHN RICHARDS, 31053

WILLIAM R. EVANS 25858

RICHARD J. STREET, 25765

JANET L. CORD, 33778

PETER D. GALLOWAY, 27885

CLIFFORD J. MASS, 30086

IAN C. BAILLIE, 24090

CYNTHIA R. MILLER, 34678

RICHARD P. BERG, 28145

(Check the following item, if applicable)

- ☐ I hereby appoint the practitioner(s) associated with the Customer Number provided below to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith.
- ☐ Attached, as part of this declaration and power of attorney, is the authorization of the above-named practitioner(s) to accept and follow instructions from my representative(s).

NOTE: Special care should be taken in continuation or divisional applications to ensure that any change of correspondence address in a prior application is reflected in the continuation or divisional application. For example, where a copy of the oath or declaration from the prior application is submitted for a continuation or divisional application filed under 37 CFR 1.53(b) and the copy of the oath or declaration from the prior application designates an old correspondence address, the Office may not recognize, in the continuation or divisional application, the change of correspondence address made during the prosecution of the prior application. Applicant is required to identify the change of correspondence address in the continuation or divisional application to ensure that communications from the Office are mailed to the current correspondence address. 37 CFR 1.63(d)(4). * Section 601.03, M.P.E.P., 7th Ed

62395

SEND CORRESPONDENCE TO

Ladas & Parry
26 West 61st Street
New York, N.Y. 10023

DIRECT TELEPHONE CALLS TO:
(Name and telephone number)

JULIAN H. COHEN
(212) 708-1887

(complete the following if applicable)

Since this filing is a ☐ continuation ☐ divisional there is attached hereto a Change of Correspondence Address so that there will be no question as to where the PTO should direct all correspondence.

DECLARATION

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

42375

SIGNATURE(S)

NOTE: Carefully indicate the family (or last) name, as it should appear on the filing receipt and all other documents.

NOTE: Each inventor must be identified by full name, including the family name, and at least one given name without abbreviation together with any other given name or initial, and by his/her residence, post office address and country of citizenship. 37 C.F.R. Section 1.63(a)(3).

NOTE: Inventors may execute separate declarations/oaths provided each declaration/oath sets forth all the inventors. Section 1.63(a)(3) requires that a declaration/oath, inter alia, identify each inventor and prohibits the execution of separate declarations/oaths which each sets forth only the name of the executing inventor. 62 Fed. Reg. 53,131, 53,142, October 10, 1997.

Full name of sole or first inventor

Zvi KAM
(Given Name) (Middle Initial or Name) Family (Or Last Name)

Inventor's signature (x) Zvi Kam

Date (x) 11/20/01 Country of Citizenship ISRAEL

Residence Hashofim Street 38, 64365 Tel Aviv ISRAEL

Post Office Address SAME AS ABOVE

Full name of second joint inventor, if any

John W SEDAT
(Given Name) (Middle Initial or Name) Family (Or Last Name)

Inventor's signature (x) John W. Sedat

Date (x) 11/27/2001 Country of Citizenship UNITED STATES

Residence 294 Yerba Buena Avenue, San Francisco, California 94127

Post Office Address SAME AS ABOVE

Full name of third joint inventor, if any

David A AGARD
(Given Name) (Middle Initial or Name) Family (Or Last Name)

Inventor's signature (x) David A. Agard

Date (x) 11/27/01 Country of Citizenship UNITED STATES

Residence 150 CHAPIN LANE, BURLINGAME, CA 94010

Post Office Address SAME AS ABOVE

42575

(check proper box(es) for any of the following added page(s)
that form a part of this declaration)

[x] Signature for fourth and subsequent joint inventors. Number of pages added 1

* * *

[] Signature by administrator(trix), executor(trix) or legal representative for deceased or incapacitated inventor. Number of pages added _____

* * *

[] Signature for inventor who refuses to sign or cannot be reached by person authorized under 37 C.F.R. Section 1.47. Number of pages added _____

* * *

[] Added page for signature by one joint inventor on behalf of deceased inventor(s) where legal representative cannot be appointed in time. (37 C.F.R. Section 1.47)

* * *

[] Added pages to combined declaration and power of attorney for divisional, continuation, or continuation-in-part (C-I-P) application.

[] Number of pages added _____

* * *

[] Authorization of practitioner(s) to accept and follow instructions from representative.

(If no further pages form a part of this Declaration,
then end this Declaration with this page and check the following item)

[] This declaration ends with this page.

42895

Practitioner's Docket No. U 013475-2ADDED PAGE TO COMBINED DECLARATION AND POWER OF
ATTORNEY FOR SIGNATURE BY FOURTH AND SUBSEQUENT INVENTORS

Full name of fourth joint inventor, if any

Bridget
(Given Name)

M

(Middle Initial or Name)

Hanser BMH

HAUSER

Family (Or Last Name)

Inventor's signature (x) Bridget HauserDate (x) 11/27/01Country of Citizenship UNITED STATES

Residence

1358 11th Ave. San Francisco, California 94122 United States

Post Office Address

SAME AS ABOVE

Full name of fifth joint inventor, if any

(Given Name)

(Middle Initial or Name)

Family (Or Last Name)

Inventor's signature

Date

Country of Citizenship

Residence

Post Office Address

Full name of sixth joint inventor, if any

(Given Name)

(Middle Initial or Name)

Family (Or Last Name)

Inventor's signature

Date

Country of Citizenship

Residence

Post Office Address

Practitioner's Docket No. U 013475-2

PATENT

Optional Customer No. Bar Code



00140

PATENT TRADEMARK OFFICE

COMBINED DECLARATION AND POWER OF ATTORNEY(ORIGINAL, DESIGN, NATIONAL STAGE OF PCT, SUPPLEMENTAL, DIVISIONAL,
CONTINUATION, OR C-I-P)

As a below named inventor, I hereby declare that:

TYPE OF DECLARATION

This declaration is of the following type:

(check one applicable item below)

- ☐ original.
☐ design.

NOTE: With the exception of a supplemental oath or declaration submitted in a reissue, a supplemental oath or declaration is not treated as an amendment under 37 CFR 1.312 (Amendments after allowance). M.P.E.P. Section 714.16, 7th Ed.

- ☐ supplemental.

NOTE: If the declaration is for an International Application being filed as a divisional, continuation or continuation-in-part application, do not check next item; check appropriate one of last three items.

- ☒ national stage of PCT.

NOTE: If one of the following 3 items apply, then complete and also attach **ADDED PAGES FOR DIVISIONAL, CONTINUATION OR C-I-P**.

NOTE: See 37 C.F.R. Section 1.63(d) (continued prosecution application) for use of a prior nonprovisional application declaration in the continuation or divisional application being filed on behalf of the same or fewer of the inventors named in the prior application.

- ☐ divisional.
☐ continuation.

NOTE: Where an application discloses and claims subject matter not disclosed in the prior application, or a continuation or divisional application names an inventor not named in the prior application, a continuation-in-part application must be filed under 37 C.F.R. Section 1.53(b) (application filing requirements-nonprovisional application)

- ☐ continuation-in-part (C-I-P).

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INVENTORSHIP IDENTIFICATION

WARNING: *If the inventors are each not the inventors of all the claims, an explanation of the facts, including the ownership of all the claims at the time the last claimed invention was made, should be submitted.*

My residence, post office address and citizenship are as stated below, next to my name. I believe that I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter that is claimed, and for which a patent is sought on the invention entitled:

TITLE OF INVENTION

COMPUTERIZED ADAPTIVE IMAGING

SPECIFICATION IDENTIFICATION

The specification of which:

(complete (a), (b), or (c))

(a) ☐ is attached hereto.

NOTE: *"The following combinations of information supplied in an oath or declaration filed on the application filing date with a specification are acceptable as minimums for identifying a specification and compliance with any one of the items below will be accepted as complying with the identification requirement of 37 C.F.R. Section 1.63:*

"(1) name of inventor(s), and reference to an attached specification which is both attached to the oath or declaration at the time of execution and submitted with the oath or declaration on filing;

"(2) name of inventor(s), and attorney docket number which was on the specification as filed; or

"(3) name of inventor(s), and title which was on the specification as filed."

Notice of July 13, 1995 (1177 O.G. 60).

(b) ☐ was filed on _____, ☐ as Application No. _____
☐ and was amended on _____ (if applicable).

NOTE: *Amendments filed after the original papers are deposited with the PTO that contain new matter are not accorded a filing date by being referred to in the declaration. Accordingly, the amendments involved are those filed with the application papers or, in the case of a supplemental declaration, are those amendments claiming matter not encompassed in the original statement of invention or claims. See 37 C.F.R. Section 1.67.*

NOTE: *"The following combinations of information supplied in an oath or declaration filed after the filing date are acceptable as minimums for identifying a specification and compliance with any one of the items below will be accepted as complying with the identification requirement of 37 C.F.R. Section 1.63:*

(A) application number (consisting of the series code and the serial number, e.g., 08/123,456);

(B) serial number and filing date;

(C) attorney docket number which was on the specification as filed;

(D) title which was on the specification as filed and reference to an attached specification which is both attached to the oath or declaration at the time of execution and submitted with the oath or declaration; or

(E) title which was on the specification as filed and accompanied by a cover letter accurately identifying the application for which it was intended by either the application number (consisting of the series code and the serial number, e.g., 08/123,456), or serial number and filing date. Absent any statement(s) to the contrary, it will be presumed that the application filed in the PTO is the application which the inventor(s) executed by signing the oath or declaration.

M.P.E.P. Section 601.01(a), 7th ed.

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- (c) ☒ was described and claimed in PCT International Application No. PCT/IL99/00645 filed on November 30, 1999 and as amended under PCT Article 19 on _____ (if any).

SUPPLEMENTAL DECLARATION (37 C.F.R. Section 1.67(b))

(complete the following where a supplemental declaration is being submitted)

☐ I hereby declare that the subject matter of the

☐ attached amendment

☐ amendment filed on _____.

was part of my/our invention and was invented before the filing date of the original application, above identified, for such invention.

ACKNOWLEDGMENT OF REVIEW OF PAPERS AND DUTY OF CANDOR

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information, which is material to patentability as defined in 37, Code of Federal Regulations, Section 1.56,

(also check the following items, if desired)

☐ and which is material to the examination of this application, namely, information where there is a substantial likelihood that a reasonable Examiner would consider it important in deciding whether to allow the application to issue as a patent, and

☐ in compliance with this duty, there is attached an information disclosure statement, in accordance with 37 C.F.R. Section 1.98.

PRIORITY CLAIM (35 U.S.C. Section 119(a)-(d))

NOTE: "The claim to priority need be in no special form and may be made by the attorney or agent if the foreign application is referred to in the oath or declaration as required by Section 1.63. The claim for priority and the certified copy of the foreign application specified in 35 U.S.C. Section 119(b) must be filed in the case of an interference (Section 1.630), when necessary to overcome the date of a reference relied upon by the examiner, when specifically required by the examiner, and in all other situations, before the patent is granted. If the claim for priority or the certified copy of the foreign application is filed after the date the issue fee is paid, it must be accompanied by a petition requesting entry and by the fee set forth in Section 1.17(i). If the certified copy is not in the English language, a translation need not be filed except in the case of interference; or when necessary to overcome the date of a reference relied upon by the examiner; or when specifically required by the examiner, in which event an English language translation must be filed together with a statement that the translation of the certified copy is accurate." 37 C.F.R. Section 1.55(a).

I hereby claim foreign priority benefits under Title 35, United States Code, Section 119(a)-(d) of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed.

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(complete (d) or (e))

- (d) ☐ no such applications have been filed.
 (e) ☒ such applications have been filed as follows.

NOTE: Where item (e) is entered above and the International Application which designated the U.S. itself claimed priority check item (e), enter the details below and make the priority claim.

**PRIOR FOREIGN/PCT APPLICATION(S) FILED WITHIN 12 MONTHS
 (6 MONTHS FOR DESIGN) PRIOR TO THIS APPLICATION
 AND ANY PRIORITY CLAIMS UNDER 35 U.S.C. SECTION 119(a)-(d)**

COUNTRY (OR INDICATE IF PCT)	APPLICATION NUMBER	DATE OF FILING DAY, MONTH, YEAR	PRIORITY CLAIMED UNDER 35 USC 119
IL	127359	1 DECEMBER 1998	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
US	09/238,225	27 JANUARY 1999	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
			<input type="checkbox"/> YES <input type="checkbox"/> NO
			<input type="checkbox"/> YES <input type="checkbox"/> NO
			<input type="checkbox"/> YES <input type="checkbox"/> NO

**CLAIM FOR BENEFIT OF PRIOR U.S. PROVISIONAL APPLICATION(S)
 (35 U.S.C. Section 119(e))**

I hereby claim the benefit under Title 35, United States Code, Section 119(e) of any United States provisional application(s) listed below:

PROVISIONAL APPLICATION NUMBER

FILING DATE

**CLAIM FOR BENEFIT OF EARLIER U.S./PCT APPLICATION(S)
 UNDER 35 U.S.C. SECTION 120**

- ☐ The claim for the benefit of any such applications are set forth in the attached ADDED PAGES TO COMBINED DECLARATION AND POWER OF ATTORNEY FOR DIVISIONAL, CONTINUATION OR CONTINUATION-IN-PART (C-I-P) APPLICATION.

U2395

**ALL FOREIGN APPLICATION(S), IF ANY, FILED MORE THAN 12 MONTHS
(6 MONTHS FOR DESIGN) PRIOR TO THIS U.S. APPLICATION**

NOTE: If the application filed more than 12 months from the filing date of this application is a PCT filing forming the basis for this application entering the United States as (1) the national stage, or (2) a continuation, divisional, or continuation-in-part, then also complete **ADDED PAGES TO COMBINED DECLARATION AND POWER OF ATTORNEY FOR DIVISIONAL, CONTINUATION OR C-I-P APPLICATION** for benefit of the prior U.S. or PCT application(s) under 35 U.S.C. Section 120.

POWER OF ATTORNEY

I hereby appoint the following practitioner(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith.

(list name and registration number)

JOSEPH H. HANDELMAN, 26179JULIAN H. COHEN, 20302JOHN RICHARDS, 31053WILLIAM R. EVANS 25858RICHARD J. STREIT, 25765JANET I. CORD, 33778PETER D. GALLOWAY, 27885CLIFFORD J. MASS, 30086IAIN C. BAILLIE, 24090CYNTHIA R. MILLER, 34678RICHARD P. BERG, 28145

(Check the following item, if applicable)

- ☐ I hereby appoint the practitioner(s) associated with the Customer Number provided below to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith.
- ☐ Attached, as part of this declaration and power of attorney, is the authorization of the above-named practitioner(s) to accept and follow instructions from my representative(s).

NOTE: "Special care should be taken in continuation or divisional applications to ensure that any change of correspondence address in a prior application is reflected in the continuation or divisional application. For example, where a copy of the oath or declaration from the prior application is submitted for a continuation or divisional application filed under 37 CFR 1.53(b) and the copy of the oath or declaration from the prior application designates an old correspondence address, the Office may not recognize, in the continuation or divisional application, the change of correspondence address made during the prosecution of the prior application. Applicant is required to identify the change of correspondence address in the continuation or divisional application to ensure that communications from the Office are mailed to the current correspondence address. 37 CFR 1.63(d)(4)." Section 601.03, M.P.E.P., 7th Ed

09050422 221301

u2395

SEND CORRESPONDENCE TO

Ladas & Parry
26 West 61st Street
New York, N.Y. 10023

DIRECT TELEPHONE CALLS TO:
(Name and telephone number)

JULIAN H. COHEN
(212) 708-1887

(complete the following if applicable)

Since this filing is a ☐ continuation ☐ divisional there is attached hereto a Change of Correspondence Address so that there will be no question as to where the PTO should direct all correspondence.

DECLARATION

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

0956422-1301
"SECRET"

42315

SIGNATURE(S)

NOTE: Carefully indicate the family (or last) name, as it should appear on the filing receipt and all other document.

NOTE: Each inventor must be identified by full name, including the family name, and at least one given name without abbreviation together with any other given name or initial, and by his/her residence, post office address and country of citizenship. 37 C.F.R. Section 1.63(a)(3).

NOTE: Inventors may execute separate declarations/oaths provided each declaration/oath sets forth all the inventors. Section 1.63(a)(3) requires that a declaration/oath, inter alia, identify each inventor and prohibits the execution of separate declarations/oaths which each sets forth only the name of the executing inventor. 62 Fed. Reg. 53,131, 53,142, October 10, 1997.

Full name of sole or first inventor

Zvi KAM
(Given Name) (Middle Initial or Name) Family (Or Last Name)

Inventor's signature (x) Zvi Kam

Date (x) 11/20/01 Country of Citizenship ISRAEL

Residence Hashofim Street 38, 64365 Tel Aviv ISRAEL ILX

Post Office Address SAME AS ABOVE

Full name of second joint inventor, if any

John W SEDAT
(Given Name) (Middle Initial or Name) Family (Or Last Name)

X Inventor's signature (x)

Date (x) Country of Citizenship UNITED STATES

Residence 294 Yerba Buena Avenue, San Francisco, California 94127

Post Office Address SAME AS ABOVE

Full name of third joint inventor, if any

David A AGARD
(Given Name) (Middle Initial or Name) Family (Or Last Name)

X Inventor's signature (x)

Date (x) Country of Citizenship UNITED STATES

Residence 283 Juanita Way, San Francisco, California 94127

Post Office Address SAME AS ABOVE

41375

(check proper box(es) for any of the following added page(s)
that form a part of this declaration)

☒ Signature for fourth and subsequent joint inventors. Number of pages added 1

* * *

☐ Signature by administrator(trix), executor(trix) or legal representative for deceased or incapacitated inventor. Number of pages added _____

* * *

☐ Signature for inventor who refuses to sign or cannot be reached by person authorized under 37 C.F.R. Section 1.47. Number of pages added _____

* * *

☐ Added page for signature by one joint inventor on behalf of deceased inventor(s) where legal representative cannot be appointed in time. (37 C.F.R. Section 1.47)

* * *

☐ Added pages to combined declaration and power of attorney for divisional, continuation, or continuation-in-part (C-I-P) application.

☐ Number of pages added _____

* * *

☐ Authorization of practitioner(s) to accept and follow instructions from representative.

(If no further pages form a part of this Declaration,
then end this Declaration with this page and check the following item)

☐ This declaration ends with this page.

42395

Practitioner's Docket No. U 013475-2

**ADDED PAGE TO COMBINED DECLARATION AND POWER OF
ATTORNEY FOR SIGNATURE BY FOURTH AND SUBSEQUENT INVENTORS**

Full name of fourth joint inventor, if any

Bridget
(Given Name)M
(Middle Initial or Name)HAUSER
Family (Or Last Name)

X Inventor's signature (x)

Date (x) _____ Country of Citizenship UNITED STATESResidence 1285 6TH Avenue, San Francisco, California 94122 United StatesPost Office Address SAME AS ABOVE

Full name of fifth joint inventor, if any

(Given Name)_____
(Middle Initial or Name)_____
Family (Or Last Name)

Inventor's signature _____

Date _____ Country of Citizenship _____

Residence _____

Post Office Address _____

Full name of sixth joint inventor, if any

(Given Name)_____
(Middle Initial or Name)_____
Family (Or Last Name)

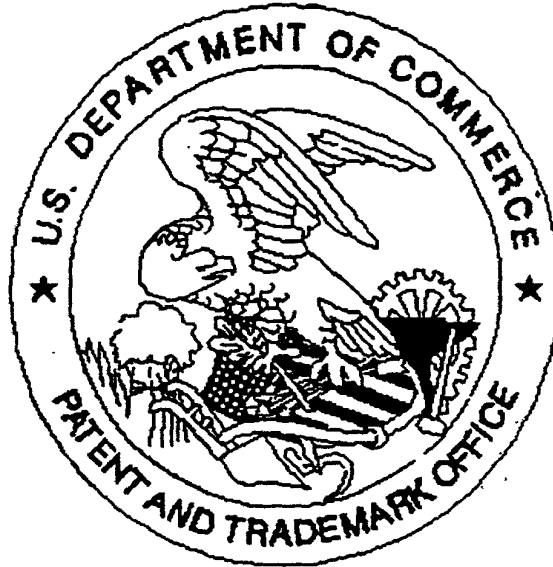
Inventor's signature _____

Date _____ Country of Citizenship _____

Residence _____

Post Office Address _____

United States Patent & Trademark Office
Office of Initial Patent Examination -- Scanning Division



Application deficiencies found during scanning:

☐ Page(s) _____ of _____ were not present
for scanning. (Document title)

☐ Page(s) _____ of _____ were not present
for scanning. (Document title)

☐ *Scanned copy is best available.* in Declaration.